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Identification of Novel Anti-inflammatory Agents from Ayurvedic Medicine for Prevention of Chronic Diseases:

"Reverse Pharmacology" and "Bedside to Bench" Approach

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Abstract

Inflammation, although first characterized by Cornelius Celsus, a physician in first Century Rome, it was Rudolf Virchow, a German physician in nineteenth century who suggested a link between inflammation and cancer, cardiovascular diseases, diabetes, pulmonary diseases, neurological diseases and other chronic diseases. Extensive research within last three decades has confirmed these observations and identified the molecular basis for most chronic diseases and for the associated inflammation. The transcription factor, Nuclear Factor-kappaB (NF-κB) that controls over 500 different gene products, has emerged as major mediator of inflammation. Thus agents that can inhibit NF-κB and diminish chronic inflammation have potential to prevent or delay the onset of the chronic diseases and further even treat them. In an attempt to identify novel anti-inflammatory agents which are safe and effective, in contrast to high throughput screen, we have turned to "reverse pharmacology" or "bed to benchside" approach. We found that Ayurveda, a science of long life, almost 6000 years old, can serve as a "goldmine" for novel anti-inflammatory agents used for centuries to treat chronic diseases. The current review is an attempt to provide description of various Ayurvedic plants currently used for treatment, their active chemical components, and the inflammatory pathways that they inhibit.

2. Introduction

Current estimates are that it may cost as much as over a billion dollar to develop a drug by a pharmaceutical company. Today's Magic bullets or targeted therapies are expensive as cost of treating advanced colorectal cancer patient that was $500 in 1999 is $250,000 in 2007 as indicated by Leonard Saltz, from Memorial Sloan-Kettering cancer Center, New York. Despite billions that have been spent, the death rate from most cancers has barely budged. For instance glioblastoma, kills almost everyone who gets it, usually in a little over a year. Radiation and chemotherapy regimen has become the standard of care, which comes with a cost range from $100,000 to $500,000. It has been estimated that most population in the world can not afford these smart therapies. Besides cost, safety is a major concern. Similarly it is being asked if someone invented a pill to cut a cancer risk in half, would you take it? Although tamoxifen, raloxifen, celcoxib and finesteride have been approved, they are not very well accepted. The reason for this being is the side effects. For instance, among 1,000 women, 19 would be expected to develop breast cancer over the next five years but if those women all took tamoxifen, however, 9 of those women would avoid breast cancer.

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Tamoxifen is expected to cause 21 additional cases of endometrial cancer, a cancer of the uterine lining that is typically treatable when caught early. An additional 21 would develop blood clots, 31 would develop cataracts and 12 would develop sexual problems. More than half of the 1,000 women would naturally develop hormonal symptoms like hot flashes, changes in vaginal discharge or irregular periods, tamoxifen would cause those symptoms in about an additional 120 women. Raloxifene has been shown to significantly reduce breast cancer risk but with fewer side effects.

To identify a drug that is safe, affordable and effective is a challenge to modern medicine today. Why modern drugs are so unsafe? Why these drugs costs so much? Why are these drugs so ineffective? All these questions require serious thinking “out of the box”. For instance the realization that most chronic diseases are multigenic and thus multi-targeted approach, also called promiscuity in drug development, is needed. As many as 500 gene products or proteins or kinases or signaling intermediates have been linked with any given chronic disease. Thus inhibition of a single kinase or a pathway is unlikely to treat the disease. It has been shown that 74% of all drugs approved by the FDA within last decade for cancer are based on natural products. How to design a drug that is safe, multi-targeted and yet affordable, we have turned to traditional medicine such as Ayurveda which is almost six thousand years old. Ayurveda is a traditional healing system originated in India approximately 6,000 years ago. In Sanskrit, Ayu means “Life” and Veda means “knowledge or science.” Ayurveda can be interpreted as the Science of Life. This “Science of Life” is a holistic healing system, which is designed to promote good health and longevity rather than curing a disease (therapy). Three kinds of primary body constitutions or traits (“prakriti”) have been defined based on three “doshas”, viz, Vata, Pitta, and Kapha. Any imbalance in these dosha results into a disease. To restore the balance, the Ayurveda recommends a customized therapy based on the “prakriti” of an individual. Doshas can be influenced by the food one eats, the type of lifestyle one leads. The term “vata” comes from “vaayu” (in Sanskrit), which means air. The oxidative stress could be caused by insufficient air (vaayu) inhaled, and imbalance in metabolism (the two other tridoshas, the pitta and the kapha). According to ‘Charaka Samhita’, there are five categories of vata. The ‘Prana vata’ is related to inhalation of air, whereas, the ‘Udana vata’ is related to exhalation. ‘Vyana Vata’ regulates the heart and circulatory system; Samana Vata regulates digestive tract, and the ‘Apana Vata’ works in elimination of wastes [1]. Since reactive oxygen species produced ROS) in the body are composed of many species, such as, oxygen ions, peroxides, hydroxyl radicals, etc.; one would require a combination of antioxidants to quench them altogether. Plant polyphenolics though are good source of antioxidants, but they differ in their abilities to quench difference species of ROS [2–4]. Therefore, one may need to use a combination of phytochemicals.

Holistic treatment is the hallmark of treatment in Ayurveda. It demands that one herb or one drug would not cure the imbalance of “Dosha”. Therefore, traditionally, in most of the cases, a combination of herbs and plants (which are even part of staple food) are recommended for treatment [5]. This would probably the most ancient recommendation for a “Combinatorial and Mutlti-targted Therapy”. It is quite possible that a so called crude herbal formulation has a combination of compounds, where one compound either potentiates the effect other, or increases the bioavailibilty, or reduces the toxicity. A best example is the routine use of turmeric in combination with black pepper as a spice. It is now known that the bioavailibity of curcumin (active ingredient of turmeric) is increased by piperine (an active compound in black pepper) by preventing the glucuronidation of the curcumin [6]. Experimentation and documentation of more of such scientific information is highly desirable, and scientific researches to substantiate the use of mixtures of plants in Ayurveda (Table 1) are a worthwhile venture.

We describe here almost 200 different plants that have been used in Ayurveda to treat various chronic diseases (Table 2; Fig. 1). The active component from some of these plants that can modify the inflammatory pathways linked to chronic diseases, are also indicated. Some of these active components have been studied by us and others extensively at the preclinical level. This approach we describe as a "reverse pharmacology"[7] or "bed to benchside" approach to validate the knowledge that has been known for long time.

Inflammatory pathways & chronic diseases

Nuclear factor-κB (NF-κB), a nuclear transcription factor, was first identified in 1986 by Sen and Baltimore [8]. As its name implies, it is a nuclear factor bound to an enhancer element of the immunoglobulin kappa light chain gene in B cells. First considered a B-cell transcription factor, NF-κB is now known to comprise a family of ubiquitous proteins. NF-κB proteins contain a Rel homology domain (DNA-binding domain/dimerization domain) with a nuclear localization sequence; such sequences are conserved from Drosophila to man. Class I proteins include p50, p52, p100, and p105. Multiple copies of ankyrin repeats are present in p100 and p105; proteolytic cleavage of p100 forms p52 and that of p105 forms p50. These protein, in turn, form dimers with class II proteins (c-Rel, RelB, and RelA/p65), which exclusively contain C-terminal activation domains. Whereas RelB forms only heterodimers, all the other proteins can form both homo- and heterodimers. NF-κB is the most common heterodimer formed between Rel A and p50. Dimeric NF-κB transcription factors bind to the 10-base-pair consensus site GGGPuNNPyPyCC, where Pu is purine, Py is pyrimidine, and N is any base. The individual dimers have distinct DNA-binding specificities for a collection of related B sites.

The various inhibitors of NF-κB include IκBα, IκBβ, IκBγ (derived from the C-terminal of p100), IκBε, Bcl-3, pp40 (a chicken homologue), cactus (a Drosophila homologue), and avian swine fever virus protein p28, p105 and p100 can also function to retain NF-κB subunits in the cytoplasm. All of these proteins are characterized by the presence of multiple ankyrin repeats. Perhaps the most common and best-understood form of NF-κB consists of p50, p65, and IκBα. IκBα mediates transient gene expression, whereas IκBβ mediates persistent response.

The IκB proteins are expressed in a tissue-specific manner and have distinct affinities for individual Rel/NF-κB complexes. IκBs contain six or more ankyrin repeats, an N-terminal regulatory domain, and a C-terminal domain that contains a proline-glutamic acid-serine-threonine motif. IκBs bind to NF-κB dimers and sterically block the function of their nuclear localization sequences, thereby causing their cytoplasmic retention. Most agents that activate NF-κB mediate the phosphorylation-induced degradation of IκB. On receipt of a signal, phosphorylation of IκBα takes place on two conserved serine residues (S32 and S36) in the N-terminal regulatory domain. However, another member of the IκB family, Bcl-3, stimulates transcription after interacting with p50 and p52 subunits of NF-κB. Several of the IκB kinases (IKKs) have been characterized, namely, IKKα, IKKβ, and IKK. Mutation analysis revealed that IKKα and not IKKβ mediates proinflammatory signals. Once phosphorylated, the IκBs, which are still bound to NF-κB, almost immediately undergo a second posttranslational modification known as polyubiquitination. The major ubiquitin acceptor sites in human IκBα are lysines 21 and 22. Protein ubiquitination occurs through the E1 ubiquitin-activating enzyme, the E2 ubiquitin-conjugating enzyme, and the E3 ubiquitin protein ligases. After ubiquitination, IκBs are degraded in 26S proteasomes, leading to the release of NF-κB dimers, which translocate into the nucleus [9]. In contrast, the activation of NF-κB in response to ultraviolet (UV) radiation is accompanied by IκBα degradation but not phosphorylation on the N-terminus of IκBa. Hypoxia or pervanadate treatment stimulates the phosphorylation of IκBα at tyrosine 42, but other IκBs do not have a tyrosine at this position. Phosphorylation on Ser-276 by the catalytic subunit of protein

kinase A contributes to the intrinsic transcriptional capacity of the p65 subunit of NF-κB. The catalytic subunit of protein kinase A was also found to be associated with NF-κB and IκB in the cytoplasm and was able to phosphorylate p65 only after IκB degradation [7]. In addition, a site-directed mutant of p65 (Ser-276 to Ala) is phosphorylated at Ser 529 in response to tumor necrosis factor (TNF), suggesting that multiple physiologic stimuli modulate p65 through distinct phosphorylation sites to control transcriptional activity. RelA (C-terminus) has been shown to interact with basal transcriptional apparatus proteins such as TATA-binding protein (TBP), transcription factor (TF) IIB and TBP-associated factor (TAF) 105 and with coactivators such as cAMP responsive element binding protein (CBP) and p300, although the actual role of these interactions is not clear [10]. This pathway is well conserved, both in structure and function, from Drosophila to humans.

NF-κB is activated by many divergent stimuli, including proinflammatory cytokines (e.g., TNF-a, interleukin-1 [IL-1]), T- and B-cell mitogens, bacteria, lipopolysaccharide (LPS), viruses, viral proteins, double-stranded RNA, and physical and chemical stresses. Cellular stresses, including ionizing radiation and chemotherapeutic agents, also activate NF-κB (Fig. 2).

Although much has been learned since the discovery of NF-κB, the precise mechanism of its activation is still not fully understood. Depending on the stimulus, this mechanism involves overlapping and nonoverlapping steps. For example, TNF, one of the most potent activators of NF-κB, interacts with the TNF receptor (TNFR) and then recruits a protein called TNFR-associated death domain. This protein binds to TNFR-associated factor (TRAF) 2, which recruits NF-κB–inducing kinase (NIK), which in turn activates IKK. IKK phosphorylates IκBa at serines 32 and 36, which leads to ubiquitination at lysines 21 and 22, and this leads to the degradation of IκBa by the 26S proteasome. This degradation results in translocation of NF-κB to the nucleus, where it binds to its consensus sequence (5′-GGGACTTTC-3′) and activates gene expression. Thus, NF-κB can be monitored by the IκBa degradation seen on Western blotting, by the NF-κB binding to DNA seen on electrophoretic mobility shift assay, or by the NF-κB–dependent reporter gene expression seen on transient transfection.

Besides the previously described canonical NF-κB activation pathway, a noncanonical NF-κB activation pathway is activated by CD40L, lymphotoxin (LT)-β, receptor activator of NF-κB ligand (RANKL), and B-cell-activating factor of the TNF family (BAFF), all members of the TNF family. This pathway does not involve IκBa but instead involves direct phosphorylation and ubiquitin-dependent degradation of p100. Current research indicates that NF-κB activation is highly complex and may involve dozens of different protein kinases. Besides NIK, IKK-α, and IKK-β, NF-κB activation may also require the involvement of other kinases, such as atypical protein kinase C, protein kinase C-z, pp90rsk, double-stranded RNA-dependent protein kinase, cot kinase (also called TPL2), mitogen-activated protein kinase kinase kinase 1, 2, and 3), phosphatidylinositol 3 protein kinase, Akt, mixed lineage kinase 3, hematopoietic progenitor kinase-1, transforming growth factor β–activated kinase 1, and c-raf kinase. These kinases may form a cascade, and different cascades may form depending on the NF-κB activator. For instance, IKK can be phosphorylated by NIK, mitogen-activated protein kinase kinase kinase, or Akt. Although IKK is required for NF-κB activation by most agents, a few (such as human epithelil receptor type 2, H_2O_2, pervanadate, x-rays, and -radiation) activate NF-κB through IKK-independent pathways. Although several signaling proteins and protein kinases have been identified recently that mediate NF-κB activation, more kinases and protein phosphatases remain to be identified. Besides the ubiquitin-dependent 26S proteasome, which has a role in IκBα degradation, other proteases have also been implicated in NF-κB activation.

The genetic deletions of different NF-κB proteins produce numerous phenotypic changes. For instance, deletion of the rel a gene induced embryonic lethality in mice, probably due to massive apoptosis in the liver. In addition, the mouse embryo fibroblasts (MEFs) from rel a-deletion mice were found to be hypersensitive to TNF-induced apoptosis. These results indicate a negative role for NF-κB in TNF-induced apoptosis. Furthermore, mice lacking the RelA subunit were brought to term only in aTNFR1-deficient background. These mice lacked lymph nodes, Peyer's patches, and an organized splenic microarchitecture, and they had a profound defect in their T-cell–dependent antigen responses. Analyses of TNFR1/RelA-deficient embryonic tissues and of radiation chimeras suggest that the dependence on RelA is manifested not in hematopoietic cells but rather in radioresistant stromal cells, which are needed for the development of secondary lymphoid organs. In contrast to the deletion of Rel A, the deletion of the IκBa gene leads to early neonatal lethality caused by inflammatory dermatitis and granulocytosis that are most likely induced by constitutive activation of NF-κB, leading to expression of the granulocyte colony-stimulating factor. Once NF-kB is activated, it causes the expression of almost 500 different gene products that includes enzymes, cytokines, adhesion molecules and other signaling intermediates closely linked with inflammation (Table 3).

NF-κ B and Chronic diseases—NF-κB activation has been implicated in a wide variety of diseases, including cancers, diabetes mellitus, cardiovascular diseases, autoimmune diseases, viral replication, septic shock, neurodegenerative disorders, ataxia telangiectasia (AT), arthritis, asthma, inflammatory bowel disease, and several other inflammatory conditions (Fig. 3). For example, activation of NF-κB by LPS may contribute to the development of septic shock because NF-κB activates transcription of the inducible nitric oxide synthase (iNOS) genes known to be involved in septic shock. Similarly, autoimmune diseases such as systemic lupus erythematosus may also involve activation of NF-κB. Additionally, in chronic Alzheimer's disease, the amyloid β peptide causes production of reactive oxygen intermediates and indirectly activates gene expression through B sites. The influenza virus protein hemagglutinin also activates NF-κB, and this activation may contribute to viral induction of cytokines and to some of the symptoms associated with influenza. Furthermore, the oxidized lipids from the low density lipoproteins associated with atherosclerosis activate NF-κB, which then activates other genes, and mice that are susceptible to atherosclerosis exhibit NF-κB activation when fed an atherogenic diet. Another important contributor to atherosclerosis is thrombin, which stimulates the proliferation of vascular smooth muscle cells through the activation of NF-κB. Finally, a truncated form of IκBa was shown to protect AT cells, which express constitutive levels of an NF-κB–like activity, from ionizing radiation. In light of all these findings, the abnormal activation or expression of NF-κB is clearly associated with a wide variety of pathologic conditions.

Ayurvedic plants, their active components and their molecular targets—Almost 200 Ayurvedic plants have been identified that exhibit anti-inflammatory activities. The active component from some of these plants is shown in Fig. 4. The molecular targets of these compounds are shown in Table 4. More specific description of these plants, active components and molecular targets are described below:

1. Abies pindrow: *A. pindrow*, known as the 'talisapatra' tree in Sanskrit and 'morinda' in Hindi, is found in abundance in the deciduous forests of Himalayas. Its leaves have been used as Ayurvedic remedy for fever, respiratory and inflammatory ailments. Anti-diabetic, anti-inflammatory, analgesic, hypnotic and anti-ulcerogenic activities in rats, hypotensive effect in dogs, and endurance enhancing in swimm stress in mice have been reported for extracts and fractions from *A. pindrow* leaves [11]. Pinitol (3-O-methyl-chiroinositol), a

component of *A. pindrow* was reported to suppress NF-κB activation both induced by inflammatory stimuli and carcinogens and constitutive NF-κB activation noted in most tumor cells. The suppression of NF-κB activation by pinitol occurred through inhibition of the activation of IκBα kinase, leading to sequential suppression of IκBα phosphorylation and degradation, p65 phosphorylation and nuclear translocation, and NF-κB-dependent reporter gene expression. The inhibition of NF-κB activation thereby led to down-regulation of gene products involved in inflammation (cyclooxygenase [COX]-2), proliferation (cyclin D1 and c-myc), invasion (matrix metalloproteinase [MMP]-9), angiogenesis (vascular endothelial growth factor; VEGF), and cell survival (cIAP1, cIAP2, X-linked inhibitor apoptosis protein [XIAP], Bcl-2, and Bcl-xL). Suppression of these gene products by pinitol enhanced the apoptosis induced by TNF and chemotherapeutic agents and suppressed TNF-induced cellular invasion [12].

2. Abrus precatorius: Leaves, roots and seeds of *Abrus precatorius*, known commonly as Jequirity, Crab's Eye, Rosary Pea, or Indian licorice are used for medicinal purposes. A tea is made from the leaves and used to treat fevers, coughs and colds. Abruquinones, the isoflavanquinones isolated from the roots have strong anti-inflammatory and antiallergic effects. Wang et al. [13] suggests that the anti-inflammatory effect of abruquinone is mediated partly by suppressing the release of chemical mediators from mast cells and partly by preventing vascular permeability changes caused by mediators.

3. Abutilon indicum: In traditional medicine, *A. indicum* is used as a demulcent, aphrodisiac, laxative, diuretic, pulmonary and sedative. The aqueous extract of the plant has antidiabetic properties, which inhibited glucose absorption and stimulated insulin secretion [14].

4. Acacia arabica: The gum of Acacia Arabica is the source of useful medicaments and used for treating gingivitis and for reducing plaque. The hypoglycemic effect was indicated that the powdered seeds of Acacia by initiating the release of insulin from pancreatic beta cells of normal rabbits [15].

5. Acacia catechu: Altavilla et al. [16] studied the anti-inflammatory activity of Flavocoxid, a mixed extract containing baicalin and catechin from *Acacia catechu* that acts as a dual inhibitor of cyclooxygenase (COX) and 5-lipoxygenase (LOX) enzymes and showed that Flavocoxid significantly inhibited COX-2, 5-LOX and inducible nitric oxide (NO) synthase (iNOS) expression in LPS-stimulated peritoneal rat macrophages.

6. Acacia farnesiana: The bark and the flowers of *Acacia farnesiana* are the parts most used in traditional medicine. Among all the isolated compounds viz., acasiane A & B, farnesirane A and farnesirane B, three diterpenes, two triterpenes, eight flavonoids, and betulinic acid showed moderate anti-inflammatory activities against five human cancer cell lines [17].

7. Achillea millefolium: It has seen historical use as a medicine for treatment of inflammatory diseases. It has been used to treat complaints such as inflammation, pain, wounds, hemorrhages, hepato-biliary disorders and gastrointestinal disturbances such as ulcer, liver cirrosis, chronic hepatitis and diabetes. Anti-tumor activity was studied by Tozyo et al. [18] and showed that achimillic acids A, B and C from *A. millefolium* were found to be active against mouse P-388 leukemia cells *in vivo*.

8. Achyranthes aspera: *Achyranthes aspera* is used in the indigenous systems of medicine for the treatment of inflammatory conditions and had hypoglycaemic effect. Its extracts are

also showed anti-inflammatory effects in carrageenin-induced paw oedema in rat [19] and exerted anti-carcinogenic effects *in vivo* two-stage mouse skin carcinogenesis [20].

9. Acorus calamus: *Acorus calamus L.*, sweet flag, is widely employed in modern herbal medicine as an aromatic stimulant and mild tonic. In Ayurveda, it is highly valued as a rejuvenator for the brain and nervous system and as a remedy for digestive disorders. This plant also exerts antidiabetic, anti-adipogenic, and hypolipidemic activities [21]. *A. calamus* also showed anti-inflammatory effects, and it might be mediated by suppression of NF-κB and interferon regulatory factor 3 (IRF3) [22]. Also, several reports indicated the neuroprotective effects of *A. calamus* in cortex of rat brain [23].

10. Adhatoda vasica: The extracts of *Adhatoda vasica* have been used to treat bronchitis, asthma, ulcer and rheumatism. Gibb [24] showed ambroxol, a natural alkaloid found in *A. vasica*, inhibited IgE-dependent basophil mediator release.

11. Aegle marmelos: The compounds, 6-methyl-4-chromanone, isolated from Aegle marmelos by Nicolis et al [25] showed inhibition of IL-8 in the IB3-1 CF cells in vitro. Cardenolide, periplogenin, isolated from the leaves of Aegle marmelos protected the doxorubicin induced cardiotoxicity and lipid peroxidation in rats by reversing the increase in serum creatine kinase-MB, glutamate-pyruvate transaminase, and tissue LPO [26]. Subramaniam et al. [27] reported that marmelin, an ethyl acetate fraction of Aegle marmelos extracts suppressed TNF-alpha-mediated activation and translocation of NF-kappaB, inhibited AKT and ERK phosphorylation both in-vitro and in tumor xenografts.

12. Allium Sativum: The possible therapeutic effects of garlic extract in the treatment of IBD patients showed that it reduced the inflammation by inhibiting cell-mediated T-helper-1 and inflammatory cytokines (TNF-alpha, IL-1alpha, IL-6, IL-8, T-cell IFN-gamma and IL-2) while upregulating IL-10 production [28]. Zare A et al [29] showed significant decrease in allergic airway inflammation levels in murine models. The water-soluble allyl sulfur-containing compound, S-Allyl-L-cysteine Sulfoxide (ACSO), have antioxidant and anti-inflammatory activities and Hui et al [30]showed it could inhibit proinflammatory cytokine-induced adhesion of monocytes to endothelial cells by inhibiting the MAPK signaling and related ICAM-1 expression. Ban JO [31]found another sulfur compound, thiacremonone inhibiting the NF-kappaB activation via interaction with the sulfhydryl group of NF-kappaB molecules, thus could be a used for the treatment of inflammatory and arthritic diseases. Keophiphath M et al [32] used 1,2-vinyldithiin on human preadipocytes to reduce Obesity, a state of chronic low-grade inflammation and found to be a novel, antiobesity nutraceutical.

13. Aloe vera: It has been used in the treatment of a variety of disorders including wounds and burns. In addition to its wound healing property *Aloe vera*, has also been shown to have antidiabetic and hypoglycemic properties [33]. Emodin is an active component from *A. vera* exerts anti-inflammatory effects. Emodin suppressed the activation of NF-κB in human umbelical vein endothelial cells (EC) in a dose- and time-dependent manner. Emodin inhibited degradation of IκB, an inhibitory subunit of NF-κB. Thus, emodin also downmodulated adhesion molecules like ICAM-1, VCAM-1, and ELAM-1 contain NF-κB binding sites in their promoter region in EC [34].

14. Alpinia galanga: *Alpinia galanga*, a plant in the ginger family, is an herb used in cooking. Grzanna et al. [35] documented that *Alpinia galanga* extract (GE) can inhibit the activation of human monocytic THP-1 cells by different proinflammatory stimuli and reduce the expression of a wide range of inflammation-related genes such as tumor necrosis factor (TNF)-α, interleukin (IL)-1β, COX-2, macrophage inflammatory proteins (MIP)-α,

monocyte chemotactic protein (MCP)-1, and chemokine ligand-10 (IP-10), in microglial-like cells in the central nervous system. The active component from this ginger, 1′-acetoxychavicol acetate (ACA), has been shown to inhibit phorbol ester-induced skin tumor promotion, azoxymethane-induced colonic aberrant crypt foci, estrogen-related endometrial carcinogenesis, hepatic focal lesions, rat oral carcinogenesis, and N-nitrosomethylbenzylamine-induced rat esophageal tumorigenesis. Ichikawa et al. [36] reported that ACA suppressed NF-κB activation induced by a wide variety of inflammatory and carcinogenic agents, doxorubicin, and cigarette smoke condensate. Suppression was not cell type specific, because both inducible and constitutive NF-κB activations were blocked by ACA. ACA did not interfere with the binding of NF-κB to the DNA, but, rather, inhibited IκB kinase activation, IκBα phosphorylation, IκBα degradation, p65 phosphorylation, and subsequent p65 nuclear translocation. ACA also inhibited NF-κB-dependent reporter gene expression activated by TNF, TNF-receptor (TNFR)-1, TNFR-associated death domain protein (TRADD), TNFR-associated factor-2 (TARF-2), and IκB kinase, but not that activated by p65. Consequently, ACA suppressed the expression of TNF-induced NF-κB-regulated proliferative (e.g., cyclin D1 and c-Myc), antiapoptotic (survivin, IAP1, IAP2, XIAP, Bcl-2, Bcl-xL, Bfl-1/A1, and FLIP), and metastatic (COX-2-2, ICAM-1, VEGF and MMP-9) gene products. ACA also enhanced the apoptosis induced by TNF and chemotherapeutic agents and suppressed invasion. Thus, ACA suppressed RANKL signaling had a potential to suppress bone loss. ACA inhibited RANKL signaling and consequent osteoclastogenesis in RAW 264.7 cells, a murine monocytic cell line through suppression of RANKL-induced NF-κB signaling pathway. ACA also inhibited the osteoclastogenesis induced by human cancer cell lines such as breast cancer, multiple myeloma, and head and neck squamous cell carcinoma [37].

15. Anacyclus pyrethrum: The root of *Anacyclus pyrethrum* or Mount Atlas daisy is mostly used in Siddha medicine. The fractions from *A. pyrethrum* showed a marked stimulating effect on the reticulo-endothelial system and increased the number of peritoneal exudate cells, and spleen cells of mice [38].

16. Andrographis paniculata: *A. paniculata*, literally ‘king of bitters’ is used in traditional Siddha and Ayurvedic systems of medicine as well as in tribal medicine in India and some other countries for multiple clinical applications, such as rheumatoid arthritis and inflammatory symptoms of sinusitis. Andrographolide, a diterpenoid lactone, and the major active principle isolated from the plant *A. paniculata*, has been shown to possess a strong anti-inflammatory activity through suppression of inflammatory mediators such as NF-κB, TNF-α, IL-6, MIP-2, iNOS and COX-2 [39]. The anti-diabetic potential of the plant extract was shown by evoked insulin secretion [40].

17. Areca catechu: Betel nut, a partial muscarinic agonist, is one of the mostly widely used substances across Asia has been hypothesized to have beneficial effects on both positive and negative symptoms of schizophrenia. The extracts from this plant has shown to hypotensive properties through its ability to inhibit the pressor responses to both angiotensin I and II [41].

18. Argyeria speciosa: *Argyreia speciosa* is an important ‘rasayana’ herb in Indian System of medicine that possessed a strong antioxidant, anti-inflammatory and anti-arthritic activity. The ethanolic extract significantly inhibited paw edema induced by carrageenan and Freund’s complete adjuvant and prevented accumulation of inflammatory cells in carrageenan-induced peritonitis [19].

19. Asparagus adscendens: The plant is a rich source of potential anti-diabetic agents. It has been reported to stimulate insulin secretion, enhance insulin action and to inhibit starch digestion [42].

20. Asparagus racemosus: Commonly mentioned as a rasayana in the ayurveda, the plant is considered to be of medicinal importance because of the presence of steroidal saponins and sapogenins in various parts of the plant. It has also been used for nervous disorders, inflammation, liver diseases and certain infectious diseases. The immunomodulating property of the plant has been shown to protect the rat and mice against abdominal sepsis. A recent study showed that potent phytochemicals present in the roots of the plant viz., phytosterols, saponins, polyphenols, flavonoids and ascorbic acid has the ability to regulate cholesterol metabolism and to improve antioxidant status in hypercholesteremic rats [43].

21. Azadirachta indica: The plant is known for its medicinal properties since ancient time. A number of phytochemical isolated chiefly from the leaves of the plant has been shown to possess immunomodulatory, anti-inflammatory, antihyperglycaemic, antiulcer, antimalarial, antifungal, antibacterial, antiviral, antioxidant, antimutagenic and anticarcinogenic properties. A recent report indicated that azadirachtin obtained from the plant possess anti-tumor property and has the potential to target NF-κB [44]. Nimbolide, a limonoid derived from the leaves and flowers of the plant has been shown to exhibit numerous biological activities including anti-cancer [45].

22. Bacopa monnieri: In the Indian system of medicine the plant is known as Brahmi. The administration of extract from the plant has been reported to significantly improve short-term and long-term memory. Bacoside-A has also been reported to prevent the occurrence of seizures and to reduce impaired peripheral nervous system in epileptic rats [46]. The methanolic extract as well as Bacoside-A isolated from the plant has been reported to possess wound-healing activity in Swiss albino rats [47].

23. Bambusa arundinacea: The leaves of the plant have been shown useful in inflammatory conditions, have the ability to heal the wound and have also been shown to check diarrhea in cattle. Manna, a crystalline substance obtained from the plant has been shown useful in ayurvedic medicine for ptosis and paralytic complaints. The methanol extract from the plant has been shown to possess antiinflammatory effect on carrgeenin-induced oedema in rats [48].

24. Bauhinia variegata: The powdered bark from the plant has been traditionally used in ayurvedic medicines as a tonic to the liver. The ethanolic extract and the roseoside (major constituent) from the plant have been reported to enhance insulin release in insulin secreting cell line [49]. The extract from the plant has been reported to exert anticarcinogenic and antimutagenic activity in swiss albino mice. The ethanol extract from the plant has also shown potential to possess chemopreventive property against N-nitrosodiethylamine induced liver tumor and human cancer cell lines [50].

25. Berberis aristata: *Berberis aristata* DC (Berberidaceae) known, as ‘daruharidra’ is an evergreen, spinescent shrub with known antichlamydial, antiplatelet, antimicrobial and hepatoprotective activity. Its root mainly contains berberine chloride, palmatine chloride. Root bark extract of the plant is taken twice a day for 1–2 weeks by the tribal people in Sikkim (a north-east state of India) and Darjeeling Himalayan regin to treat diabetes. Both the herbs are well known for their anti-inflammatory activity. Berberine has also been found to be effective in experimental herpetic uveitis [51]. Berberine was also shown to abolish NF-κB activation induced by various inflammatory agents and carcinogens. This alkaloid also suppressed constitutive NF-κB activation found in certain tumor cells. Suppression of

NF-κB activation occurred through the inhibition of phosphorylation and degradation of IκBαalpha by the inhibition of IκB kinase (IKK) activation, leading to suppression of phosphorylation and nuclear translocation of p65, and finally to inhibition of NF-κB reporter activity. Inhibition of IKK by berbeine was direct and could be reversed by reducing agents. Site-specific mutagenesis suggested the involvement of cysteine residue 179 in IKK. Berberine also suppressed the expression of NF-κB-regulated gene products involved in antiapoptosis (Bcl-xL, Survivin, IAP1, IAP2, and cFLIP), proliferation (cyclin D1), inflammation (COX-2), and invasion (MMP-9). Suppression of antiapoptotic gene products correlated with enhancement of apoptosis induced by TNF and chemotherapeutic agents and with inhibition of TNF-induced cellular invasion [52]. Thus this indicates that this medicinal plant exhibits activities against inflammation linked to most chronic diseases

26. Bergenia ligulata: Bergenia ligulata are popularly known in India as Pashanbheda. *Bergenia ligulata* (family, Saxifragaceae) has been used for centuries in South Asia, mainly India and Pakistan, for a wide range of ailments. The roots of *B. ligulata* have been used for the therapy of urinary stones, chronic ulcers, viral hepatitis, and benign prostatic hypertrophy. In addition, *B. ligulata* has anti-inflammatory and cytoprotective properties. However, the most important activities are its diuretic and lithotriptic effects.

27. Boerhaavia diffusa: *Boerhaavia diffusa* L. is commonly known as ‘Punarnava’ and its various parts are used in the treatment of cancer, jaundice, dyspepsia, inflammation, enlargement of spleen, abdominal pain and as an anti-stress agent [53, 54]. Administration of aqueous methanol extract of Boerhaavia diffusa was found to be effective in reducing the metastases formation by B167-10 melanoma cells and Punarnavine, an alkaloid from Boerhaavia diffusa enhanced the immune response against metastatic progression of B16F-10 melanoma cells in mice ([55]

28. Boswellia serrata: Extracts from Indian Ayurvedic medicinal plant Boswellia serrata (BE) contains beta boswellic acid, a pentacyclic triterpene and the active component of the gum resin (also called frankincense in European pharmacopeia) secreted by the bark of the tree. BE has been used for centuries in traditional Ayurvedic medicine for a wide variety of inflammatory diseases including inflammatory bowel disease [56] and rheumatoid arthritis [57]. BE has been shown to inhibit leukotriene biosynthesis from endogenous arachidonic acid in intact peripheral mononuclear neutrophils through the inhibition of 5-lipooxygenase (LOX), with IC50 as low as 1.5 μM[58]. Other pentacyclic triterpenes (amyrin and ursolic acid) lack this activity. Further studies revealed that the pentacyclic triterpene ring structure, hydrophilic group on C4 ring A, and 11-keto function are all essential for 5-LOX inhibitory activity [59]. By photoaffinity labeling, it was shown that BE binds to 5-LOX at a site distinct from substrate binding site [60]. BE has also been shown to inhibit leukocyte elastase with an IC50 of 15 μM [61], topoisomerase (topo) I and II α53 with affinity constant (KD) of 70.6 nM and 7.6 nM, respectively [62]. BE has been shown to inhibit the growth of a wide variety of tumor cells including glioma [63], colon cancer [64, 65], leukemia cells [66–70], human melanoma [71], hepatoma [72] and prostate cancer cells [73]. The apoptotic effects of BE are mediated through various mechanisms including inhibition of topoisomerase I and II without inhibiting DNA fragmentation [63, 69] and downregulation of cyclin D1, bcl-2, and bcl-xl. Apoptotic effects of BE in hepatoma and colon cancer cells were found to be mediated through caspase-8 activation[64, 72]. Recently BE was reported to induce death receptor (DR)-5 but not DR-4 or Fas through increased expression levels of CAAT/enhancer binding protein homologous protein (CHOP), which led to the activation of caspase-8 in prostate cancer cells [74]. BE also downregulated the expression of androgen receptor through modulation of Sp1 binding activity in prostate cancer cells [75].

The secretion and activity of matrix metalloproteinases (MMPs) from human fibrosarcoma HT-1080 cells was also found to be suppressed by BE [71]. The anti-inflammatory effects of this agent are further demonstrated by studies that showed that LPS-induced TNF production is blocked by BE [76]. Anti-proliferative and anti-inflammatory effects of BE are also mediated through the suppression of the NF-κB pathway2, [77] and STAT3 pathway [78]. Microarray analysis revealed that BE modulated 113 of 552 genes induced by TNF-a in human endothelial cells including MMP-3, MMP-10 and MMP-12 [79], and protected animals against experimental arthritis [80].

Numerous animal studies have been performed with BE. In guinea pigs, BE modulated the biosynthesis of leukotrienes and the course of experimental autoimmune encephalomyelitis (EAE)[81]. Topical application of a methanolic extract of Boswellia serrata (BE) to the backs of mice markedly inhibited TPA-induced increase in skin inflammation, epidermal proliferation, the number of epidermal cell layers, and tumor promotion in 7,12-dimethylbenz[a]anthracene (DMBA)-initiated mice [66]. BE potently attenuated experimental ileitis (inflammation of the ileum) in rats [82], an experimental model of inflammatory bowel disease (IBD). In another study, Anthoni et al [83] examined the mechanisms by which BE mediated its effects in experimental colitis. They showed that BE conferred protection in experimental murine colitis induced by dextran sodium sulfate (DSS). Clinical measurements of disease activity and histology were used to assess disease progression, and intravital microscopy was employed to monitor the adhesion of leukocytes and platelets in postcapillary venules of the inflamed colon. BE treatment significantly blunted disease activity as assessed both grossly and by histology. By using in vivo MatrigelTM plug assay, it was shown that BE inhibited bFGF-induced angiogenesis [84]. Also, Wistar rats treated with BE 14 days after inoculation of C6 tumor cells into their right caudate nuclei survived more than twice as long as untreated mice. Furthermore, when treatment was started immediately after implantation and stopped after 14 days, a higher dose of BE produced significantly smaller tumors with greater apoptotic fractions than untreated mice, suggesting that it might have both therapeutic and chemopreventive effects [85]. Toxicity studies with BE in rats and primates showed no pathological changes in hematological, biochemical, or histological parameters at doses up to 1000 mg/kg. The LD50 has been established at >2 g/kg [86].

29. Bryonia laciniosa: *Bryonia laciniosa* leaves extract have been used in traditional folk medicine to treat numerous diseases. The methanol extract of *B. laciniosa* exhibited analgesic and antipyretic activity in the tested experimental animal models. The extract showed inhibition on the hind paw oedema in rats caused by histamine and serotonin respectively [87].

30. Butea monosperma: *Butea monosperma* (Lam.) (family: Fabaceae) also known as flame of the forest or Palasa in Sanskrit, and in the traditional system of medicine known as ‘Ayurveda’, *Butea monosperma* has been used in the treatment of a variety of ailments including liver disorders. Nearly every part of *Butea monosperma* has been used as tonic, astringent, aphrodisiac and diuretic. The main constituent of its flower is butrin (7,3′,4′-trihydroxyflavanone-7,3′-diglucoside) and isobutrin (3,4,2′,4′-tetrahydroxychalcone-3,4′-diglucoside) have been shown to be hepatoprotective [88].

31. Caesalpinia bonducella: *C. bonducella* FLEMING (Caesalpiniaceae) plant is well known for its medicinal and therapeutic values in Indian Ayurveda. It possesses the anti-inflammatory, analgesic activities against ascites carcinoma and prevention of autoimmune diseases. It has also potent antipyretic and antinociceptive activities [89].

32. Caesalpinia digyna: Several members of the species of genus *Caesalpinia* are used traditionally for a wide variety of ethnomedical properties such as anti-inflammatory, antidiabetic, antioxidant and hepatoprotective [89]. The plant is one of the ingredients of an indigenous drug preparation “Geriforte”, which has been used for curing senile prurites with excellent results. The methanol extract of *Caesalpinia digyna* root exhibited strong scavenging effect on free radical and inhibition of lipid peroxidation [89].

33. Callicarpa macrophylla: *C. macrophylla* is used for treatment of rheumatic joints. Betulinic acid (BA), a pure compound from *C. macrophylla*, has been reported to be a selective inducer of apoptosis in tumor cells. It also exhibits anti-inflammatory and immunomodulatory properties. BA has been reported to suppress the activation of NF-κB activation through suppression of IκB kinase, thus abrogate the phosphorylation and degradation of IκBa. Treatment of cells with this triterpinoid also suppressed NF-κB-dependent reporter gene expression and the production of NF-κB-regulated gene products such as COX-2 and MMP-9 induced by inflammatory stimuli. Furthermore, BA enhanced TNF-induced apoptosis [90]. It also inhibits constitutive activation of STAT3 and STAT3-regulated gene products such as Bcl-xL, Bcl-2, cyclin D1 and survivin [91].

34. Calotropis procera: The latex of the plant *Calotropis procera* has been reported to exhibit potent anti-inflammatory activity against carrageenin and formalin that are known to release various mediators. Its anti-inflammatory effect is caused by inhibiting PGE2 [92].

35. Capparis Spinosa: *Capparis spinosa* has been employed as a flavoring in cooking and as a diuretic, hypertensive, and tonic (e.g., as a poultice) since ancient times. The ethanol extract from fruits of *C. spinosa* (ECS) significantly reduced the production of O_2^-, H_2O_2, and ROS. ECS exhibits a notable activity in protecting against oxidative stress and interrupting of ROS-ERK1/2-Ha-Ras signal loop, suggesting its potential protective effects against skin sclerosis [93].

36. Carum copticum: *Carum copticum.* Linn. (Family: Umbelliferae) is popularly known as Ajowan. As a traditional medicine, the seeds of this plant are made into a decoction and used for curing diarrhoeas, amoebiasis, febrile conditions and stomach disorders. It is much valued for its antispasmodic, antiseptic properties and effects against curing dyspepsia and disorders of inflammation [94]. In the Unani system, ajowan is used as an enhancer of body’s resistance. And Antiinflammatory effects of the total alcoholic extract (TAE) and total aqueous extract (TAQ) in 100 mg/kg doses from the seeds of *Carum copticum.* Linn were significantly had in acute rat model (carrageenan induced rat paw oedema) and a sub acute rat model (cotton pellet induced granuloma).

37. Casearia esculenta: *Casearia esculenta* Roxb. (Flacourtiaceae) has been a popular remedy for the treatment of diabetes mellitus and is one of the major ingredients of D-400, the largest selling antidiabetic drug in India (Himalaya Drug Company, Bangalore). The root extract from *C. esculenta* has been reported to reduce blood sugar level in animal model, and show antihyperglycemic property in a STZ-induced diabetic rats [95].

38. Cassia angustifolia: *Cassia angustifolia* are widely used against skin disorders in traditional Chinese medicine. And also has anti-inflammatory activity [96].

39. Cassia fistula: *Cassia fistula* linn (Caesalpinaceae) tree is one of the most widespread in the forests of India. The whole plant possesses medicinal properties useful in the treatment of skin diseases, inflammatory diseases, rheumatism, anorexia and jaundice. The heaptoprotective activity and the hypoglycaemic activity have been reported [97]. And anti-

inflammatory and antioxidant activities of the aqueous and methanolic extracts of the *Cassia fistula* Linn. bark were confirmed in Wistar albino rats (both acute and chronic models).

40. Cassia occidentalis: *Cassia occidentalis* L. is used to cure various diseases. This weed has been known to exert antimicrobial (antibacterial, antifungal, laxative, analgesic, chloretic and diuretic properties), hepatoprotective, anti-inflammatory, antimutagenic and anticarcinogenic activity. Anti-inflammatory effects of these extracts to lower the lipid peroxide content, γ-glutamyl transpeptidase and phospholipase A2 activity in the exudates of cotton pellet granuloma, resulting in the reduced availability of arachidonic acid, a precursor of prostaglandin biosynthesis, and/or by stabilization of the lysosomal membrane system. And target for anticarcinogenic activity is Lck (p56lck) protein tyrosine kinase [98].

41. Cassia tora: *Cassia tora L.* has been also prescribed in oriental herb medicine to treat night blindness, hypertension, hypercholesterolemia, constipation, hypoglycemic, hypolipidemic, antimutagenic}, anticlastogenicity, and antihepatotoxic activities. Several polyherbal formulations including *C. tora* seeds are available at Chinese markets for preventing the formation of atherosclerosis plaques. Recently, it was reported that emodin and obtusifolin in *Cassia tora L.* might be the components having antidiabetic functions since they exhibited a significant inhibitory activity on advanced glycation end products formation [99].

42. Cedrus deodara: The wood of *C. deodara* has been used since ancient days in Ayurvedic medical practice for the treatment of inflammations and rheumatoid arthritis, anti-cancer activity, potent disinfectant, anti-fungal properties, and analgesic activity [100].

43. Celastrus paniculatus: The oil obtained from the seeds of *Celastrus paniculatus* Willd. (Celastraceae) is largely used in Ayurvedic medicine for sedative action, as an anti-rheumatic agent, alleviation of intestinal spasms, analgesic and anti-inflammatory activities and anti-diarrhoea [101].

44. Cichorium intybus: Chicory roots have been used as a digestive aid, diuretic, laxative, and mild sedative. Additionally, hepatoprotective agents have been described in the seeds. Its aqueous, ethanolic, and methanolic extracts have been shown to affect cholesterol uptake and tumor development in mice [102], prevent immunotoxicity induced by ethanol, and have anti-inflammatory properties *in vitro* and *in vivo* [103].

45. Cinnamomum camphora: *Cinnamomum camphora* Sieb (Lauraceae) has long been prescribed in traditional medicine for the treatment of inflammation-related diseases such as rheumatism, sprains, bronchitis and muscle pains. *C. camphora* has anti-inflammatory mechanisms blocked the production of IL-1, IL-6 and the TNF-α from RAW264.7 cells and NO, PGE2 production in lipopolysaccharaide (LPS)/interferon (IFN)-γ-activated macrophages [104].

46. Cinnamomum cassia: *Cinnamomum cassia* is used to cure various diseases. This weed has been known to has antimicrobial, laxative, analgesic, chloretic, diuretic and and antidiabetic activity [105].

47. Cinnamomum zeylanicum: *C. zeylanicum* is described as having stimulant, antiflatulent, antiemetic and antidiarrhoeal properties. The principle constituent of cinnamomum bark is the volatile oil which contains cinnamic aldehyde, eugenol and terpenes. The cinnamon oil from *C. zeylanicum* ameliorated early stage diabetic nephropathy in alloxan-induced diabetic nephropathy [106].

48. Citrullus colocynthis: This cucurbitaceae is widely used in Tunisian folk medicine and it possesses therapeutic activities against a wide range of ailments including inflammatory disorders, arthritis and gout [107].

49. Commiphora wightii: Guggulsterone [4,17(20)-pregnadiene-3,16-dione] is a plant sterol derived from the gum resin (guggulu) of the tree Commiphora mukul. The resin of the C mukul tree has been used in Ayurvedic medicine for centuries to treat such ailments as obesity, bone fractures, arthritis, inflammation, cardiovascular disease, and lipid disorders [108, 109]. This steroid has been shown to bind to the farnesoid × receptor [110] and modulate expression of proteins with antiapoptotic, cell survival, cell proliferation angiogenic, and metastatic activities in tumor cells. Guggulsterone mediates gene expression through regulation of various transcription factors, including NF-κB [111], STAT-3 [112] and various steroid receptors such as androgen receptor and glucocorticoid receptors [113].

Gujral et al demonstrated the anti-arthritic and anti-inflammatory activity of gum guggul [114]. Sharma et al showed its activity in experimental arthritis induced by mycobacterial adjuvant [115]. The effectiveness of guggul for treating osteoarthritis of the knee has also been demonstrated [116]. Recent studies have shown that guggulsterone is an antagonist for bile acid receptor farnesoid × receptor (FXR) [110, 117]. Other studies have shown that guggulsterone enhances transcription of the bile salt export pump [118]Thus guggulsterone is an important regulator of cholesterol homeostasis. Meselhy et al showed that guggulsterone can suppress inducible nitric oxide synthetase (iNOS) expression induced by LPS in macrophages [119]. Because NF-κB has been implicated in obesity, inflammation, hyperlipidemia, atherosclerosis, and osteoarthritis and in the LPS-induced expression of iNOS, we speculated that guggulsterone mediates its effects, at least in part, through suppression of NF-κB activation. We have shown that guggulsterone will downregulate NF-kB activation and potentiate apoptosis induced by TNF, taxol and doxorubicin in human myeloid tumor cells [111]. Our laboratory recently showed that guggulsterone suppressed DNA binding of NF-κB induced by TNF, phorbol ester, okadaic acid, cigarette smoke condensate, hydrogen peroxide, and interleukin 1 (14). Guggulsterone also suppressed constitutive NF-κB activation expressed in many tumor cells. Through inhibition of IκBa kinase activation, this steroid blocked IκBa phosphorylation and degradation, thus suppressing p65 phosphorylation and nuclear translocation [111]. Guggulsterone downregulates expression of cyclooxygenase (COX)-2, matrix metalloprotease (MMP)-9), cyclin D1 expression, VEGF and of antiapoptotic gene products (IAP1, XIAP, Bfl-1/A1, Bcl-2, cFLIP, and survivin through the downregulation of NF-κB activation (14). Others have shown that guggulsterone alone will induce apoptosis in acute myeloid leukemia [120] and in prostate cancer cells [121] through the activation of caspases.

Guggulsterone inhibits osteoclastogenesis induced by NF-κB ligand (RANKL), and by breast tumor cells. Because guggulsterone can suppress the NF-κB activation induced by various carcinogens, our laboratory investigated whether guggulsterone could modulate RANKL signaling and osteoclastogenesis induced by RANKL or tumor cells (see appendix; [122]). We found that treatment of monocytes with guggulsterone suppressed RANKL–activated NF-κB activation (as indicated by gel-shift assay) and that this suppression correlated with inhibition of IκBα kinase and phosphorylation and degradation of IκBα, an inhibitor of NF-κB. Guggulsterone also suppressed the differentiation of monocytes to osteoclasts in a dose- and time-dependent manner. Finally, differentiation to osteoclasts induced by coincubating human breast tumor cells (MDA-MB-468) or human multiple myeloma (U266) cells with monocytes was also completely suppressed by guggulsterone. Collectively, our results indicate that guggulsterone suppresses RANKL and tumor cell–induced osteoclastogenesis by suppressing the activation of NF-κB.

50. Convolvulus pluricaulis: *Convolvulus pluricaulis* (CP) is known as Shankhpushpi (or shankapushpi), an herb that has been used in India for hundreds of years for nervous disorders such as stress, anxiety and insomnia. CP has an antiulcerogenic effect due to augmentation of mucosal defensive factors such as mucin secretion, lifespan of mucosal cells and glycoproteins rather than on the offensive factors such as acid-pepsin [123].

51. Crataeva nurvula: *Crataeva nurvula* has an antioxidant potential. SOD mimetic activity was found to be in *Crataeva nurvula*. Lipid peroxidation inhibitory potential was found to be in *Crataeva nurvala* and also showed a comparatively high NO quenching capacity [124].

52. Crocus sativus: *Crocus sativus* L. (saffron) is used in folk medicine, for example as an antiedematogenic agent. Aqueous and ethanolic extracts of saffron stigma and petal have an antinociceptive effect, as well as acute and/or chronic anti-inflammatory activity [125].

53. Cuminum cyminum: Cumin seeds (*Cuminum cyminum* L.) are largely used as a condiment or spice in Indian food. They are also medicinally useful to correct hoarseness of voice, gonorrhea, dyspepsia, and chronic diarrhea. Cumin supplementation significantly reduced the incidence and number of tumors in the colon. Cumin prevented the accumulation of lipids in tissues and optimized the excretion of fecal sterols and bile acids [126].

54. Curcuma amada: *C. amada* belonging to the family of Zingiberaceae, popularly known as mango ginger, has been known for its potent antioxidant activity. Mango ginger (*C. amada*) contains significant amounts of phenolics as both free and bound forms. Both free and bound phenolic fractions of mango ginger were found to be antioxidant and effective in inhibiting H+,K+-ATPase activity and *H. pylori* growth [127].

55. Curcuma longa: *Curcuma longa* (turmeric) has a long history of use in Ayurvedic medicine as a treatment for inflammatory conditions. Turmeric constituents include the three curcuminoids: curcumin (diferuloylmethane; the primary constituent and the one responsible for its vibrant yellow color), demethoxycurcumin, and bisdemethoxycurcumin. Curcumin (diferuloylmethane), an anti-inflammatory agent used in traditional medicine, has been shown to suppress cellular transformation, proliferation, invasion, angiogenesis, and metastasis. Curcumin suppressed TNF-induced NF-κB activation and NF-κB-dependent reporter gene expression. Such TNF-induced NF-κB-regulated gene products involved in cellular proliferation (COX-2, cyclin D1, and c-myc), antiapoptosis (IAP1, IAP2, XIAP, Bcl-2, Bcl-xL, Bfl-1/A1, TRAF1, and cellular cFLIP), and metastasis (VEGF, MMP-9, ICAM-1) were also downregulated by curcumin. COX-2 promoter activity induced by TNF was abrogated by curcumin [128, 129]. Bharti et al [130] reported that curcumin inhibited IL-6-induced STAT3 phosphorylation and consequent STAT3 nuclear translocation. Various activities of curcumin against different chronic diseases has been extensively reviewed by us and others [131–144].

56. Curcuma zedoaria: *Curcuma zedoaria* Rosc is a perennial herb found in tropical countries, such as India, Japan and Thailand. Various parts of this plant are used in Ayurveda and other folk medicines for the treatment of different ailments such as diarrhea, cancer. *C. zedoaria* has been used for phytochemical and pharmacological medicine [145].

57. Cymbopogon citratus: Cymbopogon citratus, commonly called as lemongrass, is a natural herb that contains citral and is a widely used herb as a food flavoring, as a perfume, and for its analgesic and anti-inflammatory purposes. Lemon grass intake ameliorated ileitis through decreasing lymphocyte migration by inhibiting beta7-expression in SAMP1/Yit

mice [146]The extract also showed reduction in the release of pro-inflammatory mediators TNF-alpha and NO significantly indicating an anti-inflammatory effect [147].

58. Cymbopogon martini: Antifungal efficacy of essential oils (EO) of Cymbopogon martini has been well documented. EOs displayed strong antifungal effects. EOs has been used for treatment of dermatophyte infections and may be recommended as an alternative to synthetic drug for topical application [148].

59. Cyperus rotundus: *Cyperus rotundus* (Family Cyperaceae) is used both as a functional food and as a drug. The extract exhibited high reduction capability and powerful free radical scavenging, especially against 1,1-diphenyl-2-picrylhydrazyl (DPPH) and superoxide anions as well as a moderate effect on NO [149].

60. Cyperus scariosus: *Cyperus scariosus*, Br. (Syn: C. pertenuis, Roxb.;family: Cyperaceae) is a delicate grass, growing luxuriously in damp. The brown coloured plant rhizomes have a folkloric reputation as cordial, tonic, emmenagogue, vermifuge, diuretic, diaphoretic and desiccant. It remains an important component of several prescriptions used in the native system of medicine to treat a variety of diseases including diarrhoea, epilepsy, gonorrhoea, syphilis and liver damage. The hepatoprotective activity of aqueous-methanolic extract of *C. scariosus* was investigated against acetaminophen and CCl4-induced hepatic damage [150].

61. Daemonorops draco: Dragon's blood is a non-specific name for red resinous exudations from quite different plant species endemic to various regions around the globe that belong to the genera Dracaena (Africa) and Daemonorops (South-East Asia), more rarely also to the genera Pterocarpus and Croton (both South America). Dragon's blood is used for medicinal purposes where it is endemic [151].

62. Datura metel: *Datura mete*l L. of Solanaceae family is a sub-glabrous shrubby herb found to exist throughout the world. It is frequently used in traditional systems of medicines as narcotic, anodyne and antispasmodic. The leaves of D. metel are reported to have anticholinergic activity and are used to relieve the spasm of bronchioles in asthma [152].

63. Didymocarpus pedicellata: Didymocarpus pedicellata R. Br. (Gesneriaceae) is widely used in traditional Indian medicines against renal afflictions. *D. pedicellata* extract was found to possess a high content of total polyphenolics, exhibit potent reducing power and significantly scavenge free radicals including several reactive oxygen species (ROS) and reactive nitrogen species (RNS). The extract also significantly and dose-dependently protected against Fe-NTA plus H_2O_2-mediated damage to lipids and DNA [153].

64. Dolichos biflorus: *Dolichos biflorus* has traditionally been used to dissolve existing renal calculi, provide symptom relief, and prevent recurrence. *D. biflorus* has been demonstrated that it inhibits calcium phosphate crystallization. *D. biflorus* causes the urinary magnesium increase that considered an inhibitor of stone formation [154].

65. Dysoxylum binectariferum: The fruit of this plant has anti-inflammatory, diuretic, and CNS depressant activities. The stem bark contains an alkaloid, rohitukine, which exhibited anti-inflammatory and immunomodulatory property. Flavopiridol, synthetic flavone derived from rohitukine, is known as potent inhibitor of several cyclin-dependent kinases (CDK) and undergoes Phase III clinical trial, currently. Flavopilidol has been reported that it suppressed NF-κB in a dose- and time-dependent manner in several cell types. This effect was mediated through inhibition of NF-κB signaling pathway. Flavopiridol also inhibited the expression of the TNF-induced NF-κB-regulated gene products cyclin D1, COX-2, and MMP-9 [155].

Therefore, flavopiridol suppressed TNF-induced activation of activator protein-1 (AP-1) through suppression of various mitogen-activated protein kinases, including c-Jun NH(2)-terminal kinase (JNK), p38 mitogen-activated protein kinase (MAPK), and p44/p42 MAPK. It is noteworthy that this flavone also suppressed the expression of various antiapoptotic proteins, such as IAP-1, IAP-2, XIAP, Bcl-2, Bcl-xL, and TRAF-1.Flavopiridol also inhibited the TNF-induced induction of intercellular adhesion molecule-1, c-Myc, and c-Fos, all known to mediate tumorigenesis [156].

66. Eclipta alba: The hepatoprotective effect of the ethanol/water (1:1) extract of *Eclipta alba* (Ea) has been studied at subcellular levels in rats against CCl4-induced hepatotoxicity. Ea significantly counteracted CCl4-induced inhibition of the hepatic microsomal drug metabolising enzyme amidopyrine N-demethylase and membrane bound glucose 6-phosphatase. The loss of hepatic lysosomal acid phosphatase and alkaline phosphatase by CCl4 was significantly restored by Ea. The study shows that hepatoprotective activity of Ea is by regulating the levels of hepatic microsomal drug metabolising enzymes [157].

67. Elettaria cardamomum: *Elettaria cardamomum* (Cardamom) was shown to play a wide range of health-promoting roles against various conditions such as constipation, colic, diarrhea, dyspepsia, vomiting, headache, epilepsy, and cardiovascular diseases. Cardamom was reported to exhibit spasmogenic, spasmolytic, blood pressure-lowering, vasodilator, diuretic, and sedative activities [158]. Recently, experimental evidence suggests that cardamom extracts display anti-cancer activities [159]. It has been reported that aqueous suspensions of cardamom have protective effects on experimentally induced colon carcinogenesis by virtue of their anti-inflammatory, anti-proliferative and pro-apoptotic activity.

68. Embelia ribes: The fruit of the *Embelia ribes* Burm. plant (Myrsinaceae) (called false black pepper in English, Vidanda in Sanskrit, and Babrang in Hindi languages) has been used to treat fever, inflammatory diseases, and a variety of gastrointestinal ailments for thousands of years. Embelin from *E. ribes* has been shown to have antitumor, anti-inflammatory, and analgesic properties. More recently, active principle, embelin was also identified as a cell-permeable, small molecular weight inhibitor of the X chromosome-linked inhibitor-of-apoptosis protein (XIAP), an antiapoptotic protein, through structure-based computational screening of a traditional herbal medicine three-dimensional structure database of 8221 individual traditional herbal products [160]. Embelin also inhibited activity through modulation of NF-κB activation. Embelin inhibited both inducible and constitutive NF-κB activation was abrogated by embelin. Thus, embelin inhibited sequentially the TNF-induced activation of the IκB kinase, IκBa phosphorylation, IκBa degradation, and p65 phosphorylation and nuclear translocation. Furthermore, embelin down-regulated gene products involved in cell survival, proliferation, invasion, and metastasis of the tumor. This down-regulation was associated with enhanced apoptosis by cytokine and chemotherapeutic agents [161].

69. Emblica officinalis: *Emblica officinalis* (Family: Euphorbiaceae) indigenous to India, is valued for its unique tannins and flavanoids, which contain very powerful antioxidant properties and used for the treatment of a number of diseases, such as dyslipidemia and atherosclerosis, as hepatoprotective, radioprotective, antibacterial, antitumor, and anti-inflammatory agents [162].

70. Eugenia jambolana: *Eugenia jambolana* Lam. (Myrtaceae), popularly known as *Jamun*, is being widely used to treat liver dysfunctions and diabetes by the traditional practitioners for over many centuries. This plant has been reported to have both antidiabetic as well as ulcer protective effects. The extract of jamun pulp showed hypoplycemic activity

by stimulating insulin secretion [163]. The chemical constituents of the seed of *E. jambolana* Lam. are gallic acid, ellagic acid, corilagin, ellagitannins, isoquercetin, quercetin, caffeic acid, ferulic acid, guaiacol, resorcinaldimethyl ether, lignaglucoside, veratrole, β-sitosterol, palmitic acid etc.

71. Evolvulus alsinoides: *Evolvulus alsinoides* (shankhpushpi which is considered as Medhya Rasayana) is an Ayurvedic drug used for its action on the central nervous system, especially for boosting memory and improving intellect. In the Ayurvedic system of medicine, the whole herb of 'Shankhpushpi' has been employed clinically for centuries for its memory potentiating, anxiolytic and tranquilizing properties. The crude extracts of *E. alsinoides* showed a marked reduction in inflammation and edema in adjuvant induced arthritic rat model [164].

72. Fagonia cretica: *Fagonia cretica* linn is tropical herbs and have been extensively used in the treatment of various types of haematological, hepatic, neurological and inflammatory conditions. The antioxidant and antibacterial properties *of Fagonia cretica* have also been well documented. *F. cretica* also overcome the oxidative stress mediated injury during ischemic neuronal injury via modulating the antioxidant pool of the cells [165].

73. Ferula assafoetida: *Ferula assafoetida* is used as a food spice in many Asian countries and for the treatment of asthma, bronchitis, ulcer, kidney stone, pain, and cancer in traditional herbal medicine. *F. assafoetida* L. was reported to have antitumor, antimutagenic and antiviral activities. Farnesiferol C is one of the sesquiterpene coumarin compounds isolated from the resin of *Ferula assafoetida* L., which have antitumor and antiangiogenic activity [166]. Farnesiferol C inhibits proliferation and angiogenesis by decreasing expression of CD31 and VEGF. It decreased the binding of VEGF to VEGFR1/Flt-1, but not to VEGFR2/KDR/Flk-1.It also decreased the phosphorylation of most of the kinases downstream of VEGFR2: focal adhesion kinase, Src, extracellular signal-regulated kinase 1/2, p38 mitogen-activated protein kinase, and c-*jun*-NH2-kinase without affecting AKT.

74. Ficus bengalensis: *Ficus bengalensis* Linn. Family: (Moraceae) is a very large tree distributed throughout India. It is commonly known as 'Bargad' in Hindi or 'Indian Banyan tree' and considered as holy tree of India. Information based on ethnomedicinal survey reveals that the herbal preparations of different parts of *Ficus bengalensis* had been considered as effective economical and safe treatments for curing various diseases, such as diarrhoea, respiratory disorders, certain skin diseases and diabetes. Extracts of Ficus bengalensis bark was also found to reduce allergy and stress in asthmatic condition in milk-induced leucocytosis and milk-induced eosinophilia [167].

75. Foeniculum vulgare: *Foeniculum vulgare* Mill (Fennel) belonging to the Family Apiaceae (Umbelliferae) is a perennial herb native to the Mediterranean region. Dried fruits of Fennel possess a fragrant odour and a pleasant aromatic taste. They are used for flavouring soups, meat dishes, sauces and confectionary items. The fruits are aromatic, stimulant, carminative and are considered to be useful in diseases of the chest, spleen and kidney. Anethole, a chief constituent fennel, has been shown to block both inflammation and carcinogenesis, but just how these effects are mediated is not known. One possibility is TNF-mediated signaling, which has also been associated with both inflammation and carcinogenesis. Anethole suppressed TNF-induced NF-κB activation through inhibition of IκBα phosphorylation and degradation. Anethole also blocked the NF-κB activation induced by a variety of other inflammatory agents. Besides NF-κB, anethole also suppressed TNF-induced activation of the transcription factor AP-1, c-jun N-terminal kinase and MAPK-kinase. In addition, anethole abrogated TNF-induced apoptosis as measured by both caspase

activation and cell viability [168]. The antitumor activity of anethole against Ehrlich ascites carcinoma has been reported [169].

76. Garcinia cambogia: *Garcinia cambogia*, an edible fruit native to southeastern Asia, contains large quantities of hydroxy citric acid (HCA), which has been shown to inhibit ATP citrate, suppress de novo fatty acid synthesis and food intake, and consequently decrease body weight gain. *G. cambogia* also acts as an antiulcerogenic agent by decreasing the acidity and to increasing the mucosal defence in the gastric areas [170]. Gambogic acid (GA) its active component has been shown to possess anticancer activity through targeting to histone acetyltransferases [171]. Pandey et al [172] reported that GA enhanced apoptosis induced by TNF and chemotherapeutic agents, inhibited the expression of gene products involved in antiapoptosis (IAP1 and IAP2, Bcl-2, Bcl-xL, and TRAF1), proliferation (cyclin D1 and c-Myc), invasion (COX-2 and MMP-9), and angiogenesis (VEGF), all of which are known to be regulated by NF-κB. GA suppressed NF-κB activation induced by various inflammatory agents and carcinogens and this, accompanied by the inhibition of TAK1/TAB1-mediated IKK activation, inhibited IκBα phosphorylation and degradation, suppressed p65 phosphorylation and nuclear translocation, and finally abrogated NF-κB-dependent reporter gene expression. GA also significantly inhibited HUVEC proliferation, migration, invasion, tube formation, and microvessel growth. In a xenograft prostate tumor model, GA effectively inhibited tumor angiogenesis and suppressed tumor growth with low side effects using metronomic chemotherapy with GA. Therefore, GA inhibited the activations of VEGFR2 and its downstream protein kinases, such as c-Src, focal adhesion kinase, and AKT[173].

77. Gaultheria yunnanensis: Among various species of Gaultheria, *Gaultheria yunnanensis* are used widely in the south of China to treat rheumatoid arthritis. *G. yunnanensis* displays considerable effects against Freund's complete adjuvant induced arthritis in rats, which is in concordance with clinical practice. n-Butanol extracts and both of the eluants with water and 30% ethanol produce a significant decrease in the paw edema. 30% ethanol eluants show a stronger activity than others. It also possesses analgesic and anti-inflammatory activities, which may be mediated, at least partly, through the suppression of inflammatory mediators [174].

78. Glycyrrhiza glabra: *Glycyrrhiza glabra* L. is one such medicinal plant whose dried roots and stolons form an important component of various Ayurvedic formulations. There are number of reports of *G. glabra* with anti-inflammatory, anticancer, antihepatotoxic, antimicrobial, antioxidant, anti-genotoxic, hepatoprotective, cytoprotective and cytotoxic activities. Other than these, licorice extract also has antidepressant properties. This antidepressant-like effect of liquorice extract is mediated by increase of brain norepinephrine and dopamine, but not by increase of serotonin [175].

79. Gmelina arborea: *Gmelina arborea's* decoction is used as a diuretic for loosening phlegm, as an appetite stimulant and in the treatment of various stomach disorders, fevers, skin problems and liver disorders. *G. arborea* is an important ingredient of generic Ayurvedic formulation "*Dashamularishta*" prescribed for several gynaecological disorders and used in several commercial ayurvedic preparations. *In vitro* studies on bark and fruit extracts showed antioxidant activity and protected liver slice culture cells by alleviating oxidative stress-induced damage to liver cells. *Ex vivo* studies of the extract on perfused isolated rabbit jejunum and *in vivo* studies based on castor oil-induced model proved to have activity against diarrhea in mice but at low doses [176].

80. Gossypium herbaceum: The extracts of *Gossypium herbaceum* have antimicrobial, antimutagenic and hepatoprotective properties. Gossypol is a yellow pigment, present in

Gossypium herbaceum plants, which has drawn the attention of many scientist because of its wide biological activities such as contraceptive [177] and anticancer [178].

81. Gymnema sylvestre: *Gymnema sylvestre* is a plant used in India and parts of Asia as a natural treatment for diabetes or "sweet urine." The hypoglycemic action of *Gymnema* leaves was first documented in the late 1920s. *Gymnema* is reported to increase glucose uptake and utilization and improve the function of pancreatic beta cells. *Gymnema* may also decrease glucose absorption in the gastrointestinal tract. Phytochemically the plant has been reported to contain gymnemagenin the sapogenin, gymnemic acid-III, -IV, -V, -VIII, and -IX, were isolated in pure states from the hot water extract of leaves of *G. sylvestre* [179]. Glycoside of gymnemic acid may block the absorption of sugar from the intestine and sweet taste of sugars. Plant extract also increases the number of insulin producing cells in pancreas and balance insulin level.

82. Hajarala yahuda: It is one of the main ingredients used in the ayurvedic preparation ashmarihar ras. This preparation contains other ingredients like Yava-kshara, Muli-kshara, and Shveta-parpati, and it is sold as a diuretic (http://divyaproducts.com/index.php?dispatch=products.view&product_id=9).

83. Hebenaria intermedia: It is an endangered medicinal orchid known as 'Ruddhi' in ayurveda and distributed in grassy slopes between 2000–3000 m in Himalayan region. It is one among the constituents of "Chyawanprash" an anti aging supplements, which is purely herbal in nature.

84. Hemidesmus indicus: It has been widely used in treatment of various diseases including leprosy, leucoderma, leucorrhoea, syphilis, chronic rheumatism, asthma, bronchitis, gravel and other urinary diseases. The active principles of *Hemidesmus indicus,* 2-hydroxy 4-methoxy benzoic acid and pregnane glycoside, showed antihyperlipidaemic and antidyslipidemic effects [180, 181].

85. Holarrhena antidysenterica: Most of the study on this plant shows its animicrobial effects and there are no literatures available on chronic diseases. Arseculeratne et al. [182] showed that rats treated with extracts of this plant produced liver lesions, disruption of the centrilobular veins, haemorrhage in the centrilobular sinusoids, focal hepatocellular necrosis and histopathology in the lungs and kidneys. These symptoms were compatible with the action of pyrrolizidine alkaloids.

86. Hordeum vulgare: Germinated barley foodstuffs (GBF), which are derived from brewer's spent grain are a highly safe food substance. In an acute experimental colitis model, GBF increases butyrate production in the lower intestine and prevents mucosal damage and bloody diarrhoea. Phenolic extracts from whole barley kernel possess high antioxidant, antiradical, and antiproliferative potentials [183].

87. Indigofera tinctoria: True indigo the common name for *Indigofera tinctoria* is the original sources of indigo dye and is obtained from its leaves. Indirubin, an active principle from indigo has been demonstrated that it had anti-inflammatory and anti-cancer activity through suppression of transcription factor NF-κB [184]. Sethi et al. [184] reported that indirubin suppressed NF-κB activation induced by various inflammatory agents and carcinogens. Indirubin also blocked the phosphorylation and degradation of IκBα through the inhibition of activation of IκB kinase and phosphorylation and nuclear translocation of p65. NF-κB reporter activity induced by TNFR1, TNF receptor-associated death domain, TRAF2, TAK1, NF-κB-inducing kinase, and IKKb was inhibited by indirubin but not that induced by p65 transfection. Thus, indirubin inhibited the expression of NF-κB-regulated

gene products involved in antiapoptosis (IAP1, IAP2, Bcl-2, Bcl-xL, and TRAF1), proliferation (cyclin D1 and c-Myc), and invasion (COX-2 and MMP-9). This correlated with enhancement of the apoptosis induced by TNF and the chemotherapeutic agent taxol in human leukemic KBM-5 cells. Indirubin also suppressed cytokine-induced cellular invasion.

88. Inula racemosa: It is an ornamental plant of the Asteraceae family that is used both internally, as well as externally in ayurveda. Externally it is used to dress the wounds and ulcers as the herb possesses antiseptic, antibacterial and antifungal activity and internally it is used in anorexia (loss of appetite) and dyspepsia (indigestion), cough, hiccup, bronchial asthma, reducing the excessive body fats, wound healing, amenorrhea as well as dysmenorrheal. *In vivo* study the extracts of *Inula racemosa* decreased total cholesterol, triglycerides, low-density lipoprotein cholesterol and the atherogenic index, and increased high-density lipoprotein cholesterol compared with the positive control by scavenging thiobarbituric acid reactive substances and modulating levels of reduced glutathione in liver, and superoxide dismutase and glutathione peroxidase in heart [185].

89. Ipomoea digitata: Vidhari Kand (Ipomoea digitata) comes in the plant family of sweet potato. In Ayurveda it is used as a general tonic. The leaves contain organic acids, isobutyric, (S)-2-methylbutyric, tiglic, n-decanoic, n-dodecanoic, cinnamic acids, and glycosidic acids, quamoclinic acid A and operculinic acid A [186].

90. Ipomoea nil: Ipomoea nil is a species of morning glory known as white-edge morning glory, ivy morning glory, and Japanese morning glory. Much of the medicinal uses of this plant remain unknown. The plant is much grown for its beautiful flowers and their fruits are consumed. There are many species of ipomoea, which has laxative or purgative properties. The seeds contains diterpene glycosides, and they posses moderate to mild anti cancer property against various cancer cell lines [187].

91. Lavandula stoechas: *L. stoechas* occurs naturally in the Mediterranean region. It has been used for a long time in traditional medicine as an anticonvulsant and antispasmodic. There are very limited literatures available about its medicinal properties and most of them describe about the isolation and constituents of essential oils from the lavender and its antimicrobial property. The roots contains triterpenes, 18-hydroxy-27-norolean-12,14-dien-30-al-28-oic acid and 3 beta-hydroxy-1-oxo-olean-12-ene-30-al-28-oic acid which has been evaluated for the anticancer property [188]. Apart from that there are no literatures available about its use in preventing chronic diseases.

92. Leucas cephalotes: *Leucas cephalotes*, the flowering annual herb, is a common weed, which is used in ayurveda to treat several ailments including diabetes. The ethanolic extract of leaves regulates carbohydrate and lipid metabolism and improves antioxidant status in insulin-dependent and non-insulin-dependent diabetes mellitus rats through modulating hepatic glycogen, blood urea and creatinine contents, and hexokinase and glucose-6-phosphatase activities [189].

93. Malaxis acuminate: There are no literatures available about the medicinal uses of this plant. This plant is otherwise called as Jeevak and found in India, China, and South-East Asia, at elevations up to to 1400 m. It is a small to medium sized, hot to warm growing terrestrial or lithophytic orchid. Its pseudobulbs are sweet, refrigerant, aphrodisiac, febrifuge and tonic. They are useful in haematemesis, fever, seminal weakness, burning sensations, dipsia, emaciation, tuberculosis and general debility (http://www.flowersofindia.net/catalog/slides/Jeevak.html).

94. Mangifera indica: Mango is rich in a variety of phytochemicals and nutrients such as vitamins A, C, B6, K and E, polyphenols, omega-3 and -6 poly unsaturated fatty acids and provitamin A carotenoids. The mango contains a triterpene called lupeol which shows strong anti-cancer activity by disrupting survivin/cFLIP activation, modulation of expression levels of cyclins-A, -B1, -D1, -D2, -E2, cyclin-dependent kinase (cdk)-2, CDK-inhibitor p21 and finally inducing G2/M cell cycle arrest [190]. Mangiferin, a xanthone glucoside, isolated from the leaves of *Mangifera indica* possesses significant antidiabetic, antihyperlipidemic and antiatherogenic properties [191].

95. Mentha piperita: Peppermint has a long tradition of medicinal use, with archaeological evidence placing its use as far back as ten thousand years ago. Many literatures show its anticancer and radioprotective potentials *in vivo* [192, 193]. It also posses anti-nociceptive effect against acetic acid-induced writhing and hot plate-induced thermal stimulation and also anti-inflammatory effect against xylene-induced ear oedema and cotton-pellet granuloma [194].

96. Mesua ferrea: The xanthones, mesuaxantbone-A, mesuaxanthone-B and euxanthone, that have been isolated from mesua ferrea exhibits anti-inflammatory activity in normal and adrenalectomised rats as tested by carrageenin induced hind paw oedema, cotton pellet granuloma and granuloma pouch techniques. *M. ferrea* also posses antioxidant [195], but the molecular mechanisms for its activities are yet to be elucidated.

97. Mimusops elengi: The bark, flowers, fruits and seeds of *Mimusops elengi* are generally used as astringent, cooling, anthelmintic, tonic, and febrifuge. It is mainly used in dental ailments like bleeding gums, pyorrhea, dental caries and loose teeth. Ethyl acetate extract possesses anti-ulcer activity against experimental gastric ulcers by decreasing the gastric acid secretory activity along with strengthening of mucosal defensive mechanisms [196].

98. Momordica charantia: *M. charantia* is depicted that it is helpful in treating wound, ulcer, dysmenorrhea, eczema, gout, jaundice, kidney stone, leprosy, leucorrhea, piles, pneumonia, psoriasis, rheumatism and scabies. Earlier studies performed with MC extract have demontostrated its antidiabetic, antiviral, antitumor, antileukemic, antibacterial, antihelminthic, antimutagenic, antimycobacterial, antioxidant, antiulcer, anti-inflammatory, hypocholesterolemic, hypotriglyceridemic, hypotensive, immunostimulant and insecticidal properties [197, 198].

99. Moringa oleifera: Various parts of this plant such as the leaves, roots, seed, bark, fruit, flowers and immature pods act as cardiac and circulatory stimulants, possess antitumor, antipyretic, antiepileptic, antiinflammatory, antiulcer, antispasmodic, diuretic, antihypertensive, cholesterol lowering, antioxidant, antidiabetic, hepatoprotective, antibacterial and antifungal activities. Ethanolic extract of seeds showed protection against acetylcholine-induced broncho-constriction and airway inflammation [199].

100. Mucuna pruriens: *Mucuna pruriens* seeds contain high concentrations of levodopa, a direct precursor of the neurotransmitter dopamine. It has long been used in traditional Ayurvedic Indian medicine for diseases including Parkinson's disease. This plant also showed the hypoglycaemic activitys in alloxan diabetic rats [200].

101. Nigella sativa: *N. sativa* has been used in the treatment of a variety of illnesses, including bronchial asthma, headache, dysentery, infections, obesity, back pain, hypertension, gastrointestinal problems, and eczema. Several components of black cumin have been identified, including thymoquione, thymol, thymohydroquinone, and dithymquinone. Thymoquinone (TQ), the most abundant component of black seed oil, has

been reported to exhibit antioxidant, antiinflammatory, and chemopreventive effects. For instance, TQ has been shown to suppress the proliferation of various tumor cells, including colorectal carcinoma, breast adenocarcinoma, osteosarcoma, ovarian carcinoma, myeloblastic leukemia, and pancreatic carcinoma, although it is minimally toxic to normal cells. TQ, the active principle of *N. sativa*, has been reported that it suppressed NF-κB activation induced by various carcinogens and inflammatory stimuli. The suppression of NF-κB signaling pathway led down-regulated the expression of NF-κB-regulated antiapoptotic (IAP1, IAP2, XIAP Bcl-2, Bcl-xL, and survivin), proliferative (cyclin D1, cyclooxygenase-2, and c-Myc), and angiogenic (matrix metalloproteinase-9 and vascular endothelial growth factor) gene products [10]. This led to potentiation of apoptosis induced by tumor necrosis factor and chemotherapeutic agents. Indeed, Yi et al [201] reported that TQ effectively inhibited human umbilical vein endothelial cell migration, invasion, and tube formation. TQ inhibited cell proliferation and suppressed the activation of AKT and extracellular signal-regulated kinase. Therefore, TQ blocked angiogenesis in both *in vitro* and *in vivo*, prevented tumor angiogenesis in a xenograft human prostate cancer (PC3) model in mouse, and inhibited human prostate tumor growth at low dosage with almost no chemotoxic side effects. Thymoquinone inhibited vascular endothelial growth factor-induced extracellular signal-regulated kinase activation but showed no inhibitory effects on vascular endothelial growth factor receptor 2 activation. Overall, these results indicate that TQ could be used as a potential drug candidate for cancer therapy.

102. Nardostachys jatamansi: *Nardostachys jatamansi* Jones DC (commonly named as jatamansi) is used for treatment of mental disorders, insomnia, hyperlipidemia, hypertension and heart diseases. It has protective effect in parkinsonism, epilepsy, cerebral ischemia, liver damage. Various sesquiterpenes (such as Jatamansic acid and Jatamansone) have been reported to be present in the rhizomes of the plant [202].

103. Nelumbo nucifera: Lotus has been known for a long time in Ayurvedic literature as an antipyretic, diuretic, as an astringent remedy in diarrhoea and as an aphrodisiac. The dry powder prepared from its flowers has recently been used in the treatment of Diabetes mellitus by Ayurvedic physicians. Armepavine (Arm), an active compound from *N. nucifera*, has been shown to exert immunosuppressive effects both *in vitro* and *in vivo* through inhibition of NF-κB activation pathways [203]. *In vitro*, Arm suppressed NF-κB activation and MAPK (p38, ERK1/2, and JNK) phosphorylations and *in vivo*, Arm attenuated the mRNA expression levels of col1α2, TGF-β1, TIMP-1, ICAM-1, iNOS, and IL-6 genes. Kim et al [204] has also shown the downregulation of iNOS and TNF alpha expression via NF-κB modulation another active compound, kaempferol.

104. Nyctanthes arbortristis: Traditionally, the flowers of *Nyctanthes arbortristis* are known to be effective as stomachic, carminative, astringent, antibilious, expectorant, hair tonic and are used in the treatment of piles and various skin diseases. The bark is used for the treatment of bronchitis and snakebite. *N. arbortristis* exhibits potential anti-inflammatory and antinociceptive activity by inhibiting histamine and serotonin induced edema formation and its analgesic may be due to inhibition of the action of prostaglandins [205]. Oral administration of leaf and fruit extracts from *N. arbortritis* reduced the expression of various cytokines, such as TNF-α, IL-1β and IL-6, in arthritic mice [205].

105. Ocimum sanctum: *Ocimum sanctum* commonly known as tulsi in Ayurvedic medicine has demonstrated various medicinal values predominantly by its antioxidant property. Different parts of the plant are traditionally used in Ayurveda and Siddha systems for the treatment of diverse ailments like infections, skin diseases, hepatic disorders and as an antidote for snake bite and scorpion sting. The plant has also demonstrated antidiabetic [206] and hypolipidemic effect [207]. Ursolic acid (UA), a pentacyclic triterpene acid from

O. sanctum has been reported to suppress NF-κB activation induced by various carcinogens including TNF, phorbol ester, okadaic acid, H_2O_2, and cigarette smoke. Ursolic acid inhibited degradation and phosphorylation of IκBα, IκB kinase activation, p65 phosphorylation, p65 nuclear translocation, and NF-κB-dependent reporter gene expression. The inhibition of NF-κB activation correlated with suppression of NF-κB-dependent cyclin D1, COX-2, and MMP-9 expression [208]. UA also inhibited both constitutive and IL-6-inducible STAT3 activation in a dose- and time-dependent manner in multiple myeloma cells. The suppression was mediated through the inhibition of activation of upstream kinases c-Src, JAK-1, JAK-2, and ERK1/2. Ursolic acid down-regulated the expression of STAT3-regulated gene products such as cyclin D1, Bcl-2, Bcl-xL, survivin, Mcl-1, and vascular endothelial growth factor. Finally, ursolic acid inhibited proliferation and induced apoptosis and the accumulation of cells in G1-G0 phase of cell cycle. This triterpenoid also significantly potentiated the apoptotic effects of thalidomide and bortezomib in multiple myeloma cells [209].

106. Operculina turpethum: *O. turpethum* (Family: Convolvulaceae), commonly known as trivrit or nishot in the western part of India and adjoining Pakistan, is a plant with immense ethno-medicinal value. *O. turpethum* extract is used to treat wide range of ailments. For instance, it is used to relieve periodic fevers, constipation, flatulence and colic obesity, to treat anaemia, splenomegaly, raised lipid levels and obesity. Turpethinic acids (A, B, C, D, and E) are isolated from the resin of the plant and lupeol, betulin, and β-sitosterol are isolated from the stem. Recently, their structurally related compounds like lupeol, betulin and sitosterol have been identified to posses a variety of pharmacological activities such as hepatoprotective, anticancer, and anti-inflammatory effects [210].

107. Orchis mascula: *O. mascula* has bean proved to have antihypertensive, antidyslipidemic and endothelial modulating activities [211]. These effects are mediated through multiple pathways that include direct vasodilation by calcium channel blockade and reduction of plasma lipids by inhibition of biosynthesis, absorption and secretion.

108. Oroxylum indicum: In Indian traditional medicine, the roots as well as stem bark of *Oroxylum indicum* (Family: Bignoniaceae), commonly known as ‘Syonaka’, has been used for centuries for the treatment of various gastric disorders. Oroxylum indicum used in Bangladeshi folk medicine has bean studied for its anticancer potential. Baicalein from *O. indicum* showed anti-cancer potential in leukemia cells through inducing cell cycle arrest and apoptosis [212].

109. Pandanus tectorius: *Pandanus tectorius* is a species of Pandanus (screwpine) that is native to Malesia, eastern Australia, and the Pacific Islands. The fruit can be eaten raw or cooked and is a major source of food in Micronesia, especially in the atolls. In Kiribati, pandanus leaves are used in treatments for cold/flu, hepatitis, dysuria, asthma, boils, and cancer, while the roots are used in a decoction to treat hemorrhoids. In Hawai’i the main parts used in making traditional medicines are the fruits, male flowers, and aerial roots [213]. These are used individually or in combination with other ingredients to treat a wide range of illnesses, including digestive and respiratory disorders.

110. Phyllanthus amarus: *Phyllanthus amarus* is traditionally used to treat flu, dropsy, diabetes, and jaundice, but it has also been reported to inhibit hepatocellular carcinoma development. *P. amarus* has potent free radical scavenging activity and could scavenge superoxides and hydroxyl radicals and inhibit lipid peroxides. Moreover, Kassuya *et al.*, have shown that the extract from *P. amarus* or some of the purified lignans such as phyltetralin, nirtetralin and niranthin exhibit *in vivo* and *in vitro* anti-inflammatory

properties. These anti-inflammatory properties are probably mediated through its direct ability to interact with platelet activating factor receptor binding sites [214].

111. Phyllanthus niruri: *Phyllanthus niruri is* a widespread tropical plant commonly found in coastal areas, including South East Asia, Southern India and China. Extracts of this herb have shown promise in treating a wide range of human diseases, such as dysentery, influenza, vaginitis, tumours, diabetes, diuretics, jaundice, kidney stones and dyspepsia. The plant is also useful for treating hepatotoxicity, hepatitis B, hyperglycaemia and viral and bacterial diseases. *P. niruri* has been used in Ayurvedic medicine for over 2000 years.

112. Picrorhiza kurroa: The extracts from roots and rhizomes of this plant (commonly called as katuka, kutki, or kutaki) are used to treat a variety of ailments, including fever, hepatitis, allergies, asthma, and other inflammatory diseases. Picroliv, an iridoid glycoside derived from *P. kurroa*, interfered the activation of NF-κB signal cascade. Picroliv abrogated TNF-induced activation of NF-κB thorough inhibition of IκB kinase, leading to inhibition of phosphorylation and degradation of IκBα. It also inhibited phosphorylation and nuclear translocation of p65. Further, picroliv directly inhibits the binding of p65 to DNA, which was reversed by the treatment with reducing agents, suggesting a role for a cysteine residue in interaction with picroliv. Mutation of Cys(38) in p65 to serine abolished this effect of picroliv. NF-κB inhibition by picroliv leads to suppression of NF-κB-regulated proteins, including those linked with cell survival (inhibitor of apoptosis protein 1, Bcl-2, Bcl-xL, survivin, and TNF receptor-associated factor 2), proliferation (cyclin D1 and cyclooxygenase-2), angiogenesis (vascular endothelial growth factor), and invasion (intercellular adhesion molecule-1 and matrix metalloproteinase-9). Suppression of these proteins enhanced apoptosis induced by TNF [215].

113. Pinus roxburghii: *Pinus roxburghii* (Chir Pine) named after William Roxburgh, is a pine native to the Himalaya. The turpentine obtained from the resin is antiseptic, diuretic, rubefacient and vermifuge. It is a valuable remedy used internally in the treatment of kidney and bladder complaints and is used both internally and as a rub and steam bath in the treatment of rheumatic affections. It is also very beneficial to the respiratory system and so is useful in treating diseases of the mucous membranes and respiratory complaints such as coughs, colds, influenza and TB. Externally it is a very beneficial treatment for a variety of skin complaints, wounds, sores, burns, boils etc and is used in the form of liniment plasters, poultices, herbal steam baths and inhalers. The wood is diaphoretic and stimulant. It is useful in treating burning of the body, cough, fainting and ulcers.

114. Piper chaba: The plant *Piper chaba* is a climbing, glabrous shrub available in various parts of India and Malay Islands. Furthermore, *P. chaba* is commonly used as pepper in the southern part of Bangladesh. Various parts of this plant have been extensively used in different traditional formulations including ayurveda. The root is useful against asthma, bronchitis, and consumption. The fruit is thermogenic, anthelmintic, expectorant, carminative and improves appetite and taste and is also used against asthma, bronchitis, fever, inflammation, piles, pain in the abdomen and at the anus. The fruit has stimulant and carminative properties, and is used in haemorrhoidal affections. Stem is used to alley post-delivery pain in mothers and also useful in rheumatic pains and diarrhea.

115. Piper longum: *Piper longum* (Long pepper) is a flowering vine in the family Piperaceae, cultivated for its fruit, which is usually dried and used as a spice and seasoning. The fruits contain the alkaloid piperine. *P. longum* is a component of Indian traditional medicine reported to be used as a remedy for treating gonorrhea, menstrual pain, tuberculosis, sleeping problems, respiratory tract, infection, chronic gut-related pain and arthritic conditions. Piper extracts and piperine possess inhibitory activities on prostaglandin

and leukotrienes COX-l inhibitory effect, as well as on NF-κB activation, and thus exhibit anti-inflammatory activity [216, 217].

116. Piper nigrum: Black pepper (*Piper nigrum*) is commonly used as a spice in human diets, but it is also used as a medicine, a preservative, and a perfume in many Asian countries. An extract of the active phenolic component, piperine, is well known to provide beneficial physiological effects. It stimulates the digestive enzymes of pancreas, protects against oxidative damage, lowers lipid peroxidation, and enhances the bioavailability of a number of therapeutic drugs. In addition, its anti-inflammatory activities have been demonstrated in rat models of carrageenan- induced rat paw edema, cotton pellet-induced granuloma, and a croton oil-induced granuloma pouch. Constituents of the piper species have shown *in vitro* inhibitory activity against the enzymes responsible for leukotriene and prostaglandin biosynthesis, 5-lipoxygenase and COX-1, respectively [217]. These effects of piperine seem to be beneficial for inflammatory diseases that are accompanied by severe pain; for example, rheumatoid arthritis.

117. Pistacia integerrima: *Pistacia integerrima* (Anacardiaceae) is a moderate size deciduous tree with a short stout bole widely distributed in the sub-alpine regions of Himalaya ranging from: Indus to Kumaun. The plant has been used in traditional medicine for rheumatic pain, analgesic and antipyretic effects, and analgesic and anti-inflammatory activities [218].

118. Pluchea lanceolata: *Pluchea lanceolata* is widely used for rheumatism and allied disorders, diseases of the abdomen, dyspepsia, bronchitis and inflammation. The decoction of *P. lanceolata* has been used traditionally for the treatment of arthritis. Flavanols isolated from this plant, such as quercetin and rutin are known for their antihistamine, anti-inflammatory and antiviral activities. Quercetin has been shown to mediate down-regulation of mutant p53 in human breast cancer cell lines [219] and to inhibit chemically induced carcinogenesis.

119. Plumbago zeylanica: The root of *Plumbago zeylanica* (also called Chitrak), a major source of plumbagin, has been used in the Indian medicine since the period of Charaka, from 750 BC, as an antiatherogenic, cardiotonic, hepatoprotective, and neuroprotective agent [220]. Plumbagin has been shown to exert anticancer and antiproliferative activities in animal models as well as in cells in culture. Sandur et al., suggest that plumbagin may be effective against cancer not only by suppressing invasion but also by inhibiting angiogenesis and inflammation through inhibition of the NF-κB signaling pathway [221]. Recently, plumbagin shown that it inhibited both constitutive and interleukin 6-inducible STAT3 phosphorylation in human multiple myeloma cells and this correlated with the inhibition of c-Src, Janus-activated kinase (JAK)1, and JAK2 activation. Thus, the inhibition of STAT3 singling pathway by plumbagin leading the chemosensitization of cancer cells [222].

120. Polygonatum verticillatum: *P. verticillatum* is a perennial rhizomatous herb with an extensive range through the northern Hemisiphere from Europe to the Himalayas to Siberia. The syrup of the fresh rhizome of this plant is used in the treatment of pain, pyrexia, burning sensation and for phthisis. Other ethnobotanical uses of the plant include as emollient, aphrodisiac, vitiated condition of pitta and vata, appetizer and tonic, galactagogue (increases milk release) and weakness. Recently, this plant also reported its antinociceptive activity [223].

121. Pongamia pinnata: *Pongamia pinnata* is a medium sized glabrous tree, found throughout India and further distributed eastwards, mainly in the littoral regions of South Eastern Asia and Australia. The seed and seed oil of this plant have been used for treating

various inflammatory and infectious diseases such as leucoderma, leprosy, lumbago, muscular and articular rheumatism. The leaves are hot, digestive, laxative, anthelmintic and cure piles, wounds and other inflammations [224].

122. Prunus amygdalus: *Prunus amygdalus* is a species of tree native to the Middle East. Claimed health benefits of this plant include improved complexion, improved movement of food through the colon (feces) and the prevention of cancer. In Ayurveda, *P.amygdalus* is considered a nutritive for the brain and nervous system. Recent studies have shown that the constituents of this tree have anti-inflammatory, immunity boosting, and anti-hepatotoxicity effects [225].

123. Pseudarthria viscida: In Ayurvedic medicines, this plant is namely, 'Dashamoola' 'Mahanarayana Taila' and 'Dhantara Taila'. It is used to treat vitiated conditions of pita and vata, asthma, tuberculosis, helminthiasis, dyspepsia, diarrheas, neurasthenia, diabetes, cardiopathy, hyperthermia and general debility and as a nasal drop in headache. The ethanol-induced gastric ulceration in mice was significantly reduced by oral administration of *P. viscida* extract [226].

124. Psoralea corylifolia: The seeds of *Psoralea corylifolia* (Babchi) contain a variety of coumarins including psoralen with medicinal uses. Psoralen plus UVA (PUVA) is used as a very effective treatment modality for various diseases, including psoriasis, eczema, vitiligo and cutaneous T-cell lymphoma. PUVA-induced immune suppression and/or apoptosis are proposed to be responsible for the therapeutic potential [227].

125. Pterocarpus marsupium: Parts of this plant (heart wood, leaves, flowers) have long been used for their medicinal properties in Ayurveda. The heartwood is used as an astringent and in the treatment of inflammation and diabetes. A multicentric study has shown that a preparation from the plant is effective in reducing levels of blood glucose and glycosylated haemoglobin in patients with non-insulin-dependent diabetes mellitus. Extract from the plant has been reported to selectively inhibit COX-2 [228].

126. Pterocarpus santalinus: It is indigenous to the Indian Peninsula and is chiefly of importance from its yielding the red dye-wood known as red saunders. The heartwood obtained from the plant has various medicinal properties, as a cooling agent, antipyretic, anti-inflammatory, anthelmintic, tonic, hemorrhage, dysentery, aphrodisiac, to treat eye diseases, mental aberrations and ulcers. In a recent study, ethanolic extract obtained from the bark of plant was found to decrease hyperglycemia by increasing glycolysis and decreasing gluconeogenesis in streptozotocin-induced diabetic rats [229].

127. Pueraria tuberosa: It is a perennial climber, growing throughout tropical parts of India. In the Ayurvedic system of medicine, the plant is used as a drug of choice to manage pain, inflammation and other related diseases. The Chayawanprash, one of the popular ayurvedic formulations with powerful anti-oxidant potential contains the plant extract as active component.

128. Punica granatum (Pomegranate): The tree represents a phytochemical reservoir of heuristic medicinal value. The seed, juice, peel, leaf, flower, bark, and roots of the plant have pharmacologic activity. The juice and peel possess anticancer activities, including interference with tumor cell proliferation, cell cycle, invasion and angiogenesis. Some of the known compounds with anti-cancer and anti-inflammatory activity obtained from the plant include -tocopherol, ursolic acid, punicic acid, hydroxycinnamic acids, quercetin, ellagitannins, flavonols, flavones, apigenin, maslinic acid and asiatic acid. Ellagitannins, and punicalagin from pomegranate have been reported to inhibit cancer cell proliferation and

apoptosis through the modulation of NF-κB signaling pathway and suppression of NF-κB-regulated gene expression. Juice (PJ), total pomegranate tannin extract (TPT) and punicalagin from pomegranate significantly suppressed TNFα-induced COX-2 protein expression. Additionally, PJ reduced phosphorylation of the p65 subunit and inhibited NF-κB DNA-binding. TPT and punicalagin, also, suppressed NF-κB DNA-binding, whereas ellagic acid was ineffective. PJ also abolished TNFα-induced AKT activation, needed for NF-κB activity. Therefore, the polyphenolic phytochemicals in the pomegranate can play an important role in the modulation of inflammatory cell signaling in colon cancer cells [230].

129. Putranjiva roxburghii: It is a moderate-sized, evergreen tree, growing up to 12 m in height. The pollen from the plant has been found an important aeroallergen for type I hypersensitivity. The leaf extract from the plant has shown potential as antinociceptive, antipyretic, and anti-inflammatory activities in mice [231].

130. Quercus infectoria: It is a small tree, most abundant in Asia Minor, and extends up to middle Asia. The galls of the plant possess pleiotropic therapeutic activities, with particular efficacy against inflammatory diseases. Oral administration of gall extract from the plant has been reported to significantly inhibit carrageenan, histamine, serotonin and prostaglandin E2 (PGE2) induced paw oedemas, while topical application of gall extract has the ability to inhibit phorbol-12-myristate-13-acetate (PMA) induced ear inflammation in various *in vivo* and *in vitro* experimental models [232].

131. Raphanus sativus: It is a cruciferous plant, rich on flavonoids, isothiocyanates, and phenolic acids and has potential as anti-inflammatory and immunomodulatory agent both in vitro and in vivo. The granules from the plant have shown potential to act as anti-inflammatory agent in a high fat diet fed rat model [233].

132. Rauwolfia serpentina: *R. serpentina* is a tropical woody plant of the Apocyanaceae family ingenious to Asia, South America and Africa. Extracts of different parts of the plant had been used in Hindu medicine for snakebite, insomnia, insanity and many other diseases. It is one of the fundamental herbs used in traditional Chinese medicine. It is also one of the main ingredients in the ayurvedic formulation ‘Divya Mukta Vati’ used to cure high blood pressure. The plant contains a number of bioactive components, including ajmaline, deserpidine, rescinnamine, serpentinine and reserpine. Reserpine, an alkaloid from Rauwolfia serpentina, was widely used for its antihypertensive action and single dose of R. serpentina formulation is effective, showed by Leary et al [234] in a double-blind placebo-controlled investigation. In animal models reserpine has been reported to significantly reduce inflammation [235, 236].

133. Ricinus communis: Commonly known as castor oil plant, it is indigenous to the southeastern Mediterranean Basin, Eastern Africa, and India. The seed from the plant is a rich source of triglycerides (mainly ricinolein) and ricin. The oil obtained from the seed of the plant has been used as a laxative, purgative, and cathartic in Unani, Ayurvedic and other ethnomedical systems. Traditional Ayurvedic medicine considers castor oil the king of medicines for curing arthritic diseases. In a study carried out in guinea-pig eyelid, ricinolein was found to possess both pro-inflammatory and anti-inflammatory properties that were observed upon acute and repeated application of the compound, respectively [237].

134. Rosa centifolia: The plant is particular to the French city of Grasse. It is widely cultivated for its singular fragrance - clear and sweet, with light notes of honey and green earth. The plant is one of the ingredients in ayurvedic formulations ‘Divya udarakalpa curna’, ‘Divya Curna’, ‘Divya peya’, ‘Himalaya abana’. The flowers are commercially

harvested for the production of rose oil, which is commonly used in perfumery. In a study, the plant was found effective in decreasing the severity of menstrual cramps in women[238].

135. Rosa damascena: The plant is a rose hybrid, derived from Rosa gallica and Rosa moschata and grows as deciduous shrub. *R. damascena* has been reported to exert antidiabetic, antiolytic and to use for treating ophthalmic disorders. The roxyloside A (flavonoid) obtained from the plant was shown potential of inhibiting 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase system and was proposed to be effective in improving the cardiovascular system [239]. The oil from the plant has been quoted extensively in ancient literature as being an anxiolytic treatment.

136. Roscoea alpina: It is a common Himalayan wildflower and occurs most frequently in open woodlands and on rocky slopes. It is one of the main ingredients in the ayurvedic formulation 'Divya pidantaka taila' used for relieving joint pain, cervical spondylitis, trauma, oedema and inflammation.

137. Rubia cordifolia: It is a flowering plant belonging to the family Rubiaceae. It is a common medicinal plant used in the preparation of different formulations in Ayurveda. The root of the plant is commonly known as Manjistha and its dried samples are sold in the market under the name Manjith. The roots of the plant are used as anti-inflammatory, haemostatic, antidysentric, antipyretic, analgesic and the anthelmentic agent. It is also used in the cure of leucoderma, ulcers, urinary discharges, jaundice, and piles. Mollugin, one of the active compounds obtained from the plant was recently shown to inhibit TNF--induced expression of inflammatory molecules by inhibiting NF-κB activation in colon cancer cells [240].

138. Rumex maritimus: It is one of the ingredients in the ayurvedic formulation 'Himalayan Diabecon' that has potential to lower blood sugar levels and minimizing long-term diabetic complications. Leaves are applied to burns; seeds are tonic and remove pain from the back. The methanol extract from the root of the plant has shown antidiarrhoeal activity in mice [241].

139. Salvadora persica: The plant has been used for centuries as a natural toothbrush and contains a number of medically beneficial properties including abrasives, antiseptics and astringent. The plant has been shown to contain trimethylamine salvadorine, chloride, fluoride, silica, sulphur, vitamin C, resins and traces of tannins, saponins, flavonids and sterol. The plant has also been shown to possess antiulcer activity in an experimental rat model [242].

140. Santalum album: It is a small tropical tree of the Santalaceae family and has been utilised, cultivated and traded for many years, some cultures placing great significance on its fragrant and medicinal qualities. Plant has been the primary source of sandalwood. The wood from the plant has been shown effective against kidney and urinary disorders. The sandalwood oil obtained from the plant has been used as aromatherapy agent to relieve anxiety, stress, and depression [243].

141. Sapindus trifoliatus: A thick aqueous solution of the pericarp from the plant is used for the treatment of hemicrania, hysteria or epilepsy in folklore medicine. The aqueous extract of the plant has shown antihyperalgesic activity by antagonising dopamine D2 activity in mice [244]. The ethanolic extract from the seeds of the plant has shown anti-inflammatory activity in wistar rats [245].

142. Saraca asoca: *Saraca asoca* (local names: Ashok, Anganapriya, etc.) is a medicinal plant whose bark is astringent and used in menorrhagia, bleeding haemorrhoids, haemorrhagic dysentery, bone fractires, strangury, vesical calculi, hyperdypsia, and inflammation. This plant is known to contain tannins, flavonoids, proanthocyanidins and leucoanthocyanidins in the bark. Two procyanidin dimers from *S. asoca* have shown the inhibitory effect of prostaglandin H2 (PGH2) synthetase [246].

143. Saraca indica: It is known to be useful for uterine disease, internal piles, diabetes, dyspepsia, indigestion, burning sensation, blood disorders, fractures, tumors, bites, ulcerations, and skin discoloration. The lectin saracin, purified from *Saraca indica* seed integument, has been found to agglutinate human lymphocytes and erythrocytes [247].

144. Saussurea lappa: *S. lappa is* considered as antiseptic, astringent, diuretic, aphrodisiac, antispasmodic, antihelmentic, and sedative and are used for the treatment of asthma, dyspepsia, rheumatism, cough, throat infections, tuberculosis, leprosy, malaria, convulsions, fever, helminth infestation and many other diseases. It is also used as a part of preparation for the treatment of various liver disorders. Recently, this plant is reported that it had antiulcer, anti-inflammatory and antiarthritic activates [19, 248].

145. Saxifraga ligulata: This plant is reported to be helpful in dissolving kidney stones and urinary antiseptic in action. In lower doses, the extract is mildly diuretic.

146. Sesamum indicum: The seeds of *S. indicum* (sesame) are used as a demulcent in respiratory affections, infantile cholera, diarrhea, dysentery and other bowel affections and bladder diseases. The seed powder is known to be benefit in amenorrhea, dysmenorrhea, ulcers and bleeding piles. The active component sesaminol is reported to its antioxidative, neuroprotective effects. Other lignan from sesamne, sesamol, has been offered protection against increased blood pressure, hyperlipidaemia [249]. Recently, Harikumar et al [250] found that sesamin, lignan from *S. indicum*, inhibited the proliferation of a wide variety of tumor cells including leukemia, multiple myeloma, and cancers of the colon, prostate, breast, pancreas, and lung. Sesamin also potentiated TNF-induced apoptosis and this correlated with the suppression of gene products linked to cell survival (Bcl-2 and survivin), proliferation (cyclin D1), inflammation (COX-2), invasion (MMP-9, ICAM-1), and angiogenesis (VEGF). Sesamin downregulated constitutive and inducible NF-κB activation induced by various inflammatory stimuli and carcinogens, and inhibited the degradation of IκBα, through the suppression of phosphorylation of IκBα and inhibition of activation of IκB kinase, thus resulting in the suppression of p65 phosphorylation and nuclear translocation.

147. Sida cordifolia: It is reported to possess analgesic, anti-inflammatory, anticancer, diuretic, laxative, hypoglycemic and hepatoprotective activities. Further, studies showed that aqueous fraction of hydroalcoholic extract of leaves induce vasorelaxation, hypotension and bradycardia. This plant also used for treatment of Parkinson's disease and as an anti-rheumatic agent and CNS depressant. The plant alkaloid cryptolepine from *S. cordifolia* has been reported to induces cell cycle arrest in a human osteosarcoma cell line [251]

148. Solanum indicum (syn. Solanum anguivi): *S. indicum* has been used on treatment of hypertension and diabetics. The steroidal glycosides from fruits have been claimed in folk medicine to have an antihypertensive effect [252] and anticancer effect [253].

149. Solanum nigrum: This plant is known as 'Black nightshade' that have been extensively used to cure liver disorders, chronic skin ailments (psoriasis and ringworm), inflammatory conditions, painful periods, fevers, diarrhoea, eye diseases, hydrophobia, etc.

The plant contains glycoalkaloids (solanine, solamargine, solanigrine and solasodine), steroidal glycosides (β-solamargine, solasonine and α,β-solansodamine), diosgenin, gitogenin, tannin and polyphenolic compounds. The fruits are commonly used as hepatoprotective agents [254], which also afford protection against free radical mediated damage.

150. Solanum xanthocarpum: *S. xanthocarpum* are known for several medicinal uses like anthelmintic, antipyretic, laxative, antiinflammatory, antiasthmatic and aphrodisiac activities. The stem, flowers and fruits are prescribed for relief in burning sensation in the feet accompanied by vesicular eruptions. The hot aqueous extract of dried fruits is used for treating cough, fever and heart diseases. Results from pilot study with patient having allergy and asthma showed that *S. xanthocarpum* relived the bronchial asthma by bronchodilating effect, reducing the bronchial mucosal edema, and/or reducing in the secretions within the airway lumen [255].

151. Sphaeranthus indicus: *S. indicus*, commonly called Gorakhmundi (in Hindi), is plant is known to possess various medicinal properties. It is reported to use in epileptic convulsions, mental illnesses and hemicranias. It is also used to treat vitiated conditions of jaundice, diabetes, leprosy, fever, pectoralgia, cough, gastropathy, hernia, haemorrhoids, helminthiasis, dyspepsia, skin diseases and as a nerve tonic. The oil from the plant root has been used to treat scrofula and as an aphrodisiac, while the external application of the herb paste has been reported to use treatment for pruritus, oedema, arthritis, filariasis, gout and cervical adenopathy [256].

152. Stereospermum suaveolens: *Stereospermum suaveolens* is a medicinal tree species and various parts of the plants are used by traditional healers, rural communities and pharmaceutical companies as a remedy for vomiting, eructation, piles, acidity, diarrhoea, gonorrhoea, loss of taste, malaria and other fevers. Balasubramanian et al [257] showed that ethanol extract of Stereospermum suaveolens possesses maximum anti-inflammatory activity in various rat models of carrageenan-, dextran-, and histamine-induced hind paw edema, and cotton pellet-induced granuloma formation in a dose-dependent manner.

153. Strychnos nuxvomica: The dried seeds of *S. nuxvomica* have been claimed to improve blood circulation and relieve rheumatic pain. Historically, this plant has been widely used in treating diseases, such as tumor and rheumatic arthritis. It also has been used in gastro-hepatic disease and as analgesic, stimulant. Indeed, it also used to treatment of paralysis, diabetes, gonorrhea, anemia and bronchitis etc. Brucine and brucine N-oxide from this plant are reported to exert anti-inflammatory effects through reduction of prostaglandin E2 release [258].

154. Swertia chirata: This plant is known as ‘Chirata’, and multifarious therapeutic value. It is used as an antimalarial, a bitter stomachic, anthelmintic, and as a remedy for scanty urine, epilepsy, ulcer, bronchial asthma and certain type of mental disorder. Studies on the biological activities of *S. chirata* extract reveal that this bitter plant possesses antioxidant, antidiabetic, antimicrobial, anticholinergic and chemopreventive activity. It contains mangiferin along with various secoiridoid glycosides (i.e. amarogentin, amaroswerin, sweroside and swertiamarin). The secoiridoid glycoside, amarogentin, is reported suppressing COX-2 [259]and also possesses various biological activities such as chemopreventive, antibacterial, anticholinergic and antihepatitis activity.

155. Symplocos crataegoides (syn. Symplocos paniculata): *S. crataegoides* has been used for treatment of menorrhagia, eye diseases, bowel complaints, dysentery, inflammations, vaginal discharges, leprosy and ulcers, as a gargle for giving firmness to spongy and

bleeding gums. And its bark juice is also used to sprains and muscular swellings. The ursane-type triterpenes from this plant showed that the inhibitory effect on protein tyrosine phosphatase 1B (PTP1B) has been proposed as a therapy for treatment of type 2 diabetes and obesity [260].

156. Syzygium aromaticum: Traditionally, it has been used to treat respiratory and digestive ailments. Cloves are used as a carminative, to increase hydrochloric acid in the stomach and to improve peristalsis. Cloves are also said to be a natural anthelmintic. The aqueous clove infusion was showed antiseptic and antibiotic properties, clove is used to treat toothache and as an ingredient in a popular toothpaste and mouthwash in India. An anti-herpes virus compound eugenin was purified from clove, which could inhibit viral DNA synthesis. In addition water extracts of clove have shown the inhibitory effect on hepatitis C virus protease. Eugenol, the principle component of clove has been shown to oxygen radical scavenging activity and antitumor potentials targeting COX-2, cMyc, H-ras [261]

157. Syzygium cumini: The bark of the plant is astringent to the bowels, sweet, refrigerant, carminative, diuretic, digestive, antihelminthic, febrifuge, constipating, stomachic and antibacterial. The fruits and seeds are used to treat diabetes, pharyngitis, spleenopathy, urethrorrhea and ringworm infection. The leaves have been extensively used to treat diabetes, constipation, leucorrhoea, stomachalgia, fever, gastropathy, strangury, and dermopathy and to inhibit blood discharges in the faeces. This plant has been also reported to poses acetyl oleanolic acid, triterpenoids, ellagic acid, isoquercitin, quercetin, kaempferol and myricetin in different concentrations. Recently, *S. cumini* also shown that the protective effect against radiation-induced DNA damage in human peripheral blood lymphocytes [262].

158. Tamarix gallica: This plant is commonly kwon as “Jhau”, s shrub of the family Tamaricaceae. The fruits and leaves have been employed in traditional medicine as an astringent for dysentery and chronic diarrhea, aperitif, stimulant of perspiration, diuretic, active against leucoderma, spleen trouble and eye diseases. Indeed, methanolic extract of this halophyte was investigated for its anti-carcinogenic and chemopreventive activities by evaluating the levels of hepatic antioxidant defense [263].

159. Terminalia arjuna: Arjuna bark (*Terminalia arjuna*) is a medicinal plant of the genus Terminalia, widely used in functional heart problems including angina, hypertension and deposits in arteries. It has been also useful in treatment of angina pectoris, heart failure, coronary artery disease and hypercholesterolemia. *In vivo* study showed its anti-inflammatory, immunomodulatory and antinociceptive activity in mice and rats [264]. In clinical study, terminalia had shown decreases platelet activation which ultimate leads in antithrombotic properties [265].

160. Terminalia belerica: *Terminalia belerica* has been used for its lowering serum glucose level and antioxidant activity by reducing lipid peroxidation, scavenge hydroxyl radical and superoxide radicals. This plant has been used for treatment of digestive and liver disorders. It can significantly reduce the total cholesterol, low density lipoprotein (LDL), very low density lipoprotein (VLDL), high density lipoprotein (HDL) and free fatty acid in experimentally induced hypercholesteremic rats [180, 266].

161. Terminalia chebula Retz: *Terminalia chebula* Retz. (Combretaceae) have been known from ancient times and were described by Charaka in his text “Charaka Samhita”. It contains the active ingredient chebulagic acid. Aqueous extract of Terminalia chebula had shown numbers of activity such as digestive, allergic and infectious diseases like cough and skin disorders, antimicrobial activity anti-diabetic and antioxidant properties [267]. It also

reported to have strong anti-anaphylactic actions, anti-inflammatory and analgesic properties [268].

162. Thymus vulgaris: *Thymus vulgaris* (*Lamiaceae*) is aromatic plants, which is distributed in subtropical countries. It contains acetophenone glycosides, phenols, thymol (40%) and carvacrol (15%). It is mainly used in smooth muscle relaxing effect, asthma, bronchitis and other respiratory diseases [269]. Thymol significantly reduced the level of DNA damage induced in K562 cells by the strong oxidant H2O2 [270].

163. Tinospora cordifolia: *Tinospora cordifolia* mainly contain different type of aporphine alkaloids and clerodane diterpenes. It is also used as an adjuvant for the prevention and/or management of insulin resistance and disorders related to it. Epoxy clerodane diterpene which obtained from it, also used against diethylnitrosamine-induced hepatocellular carcinoma [271]. Octacosanol isolated from Tinospora cordifolia downregulates VEGF gene expression by inhibiting matrix metalloproteinases and nuclear translocation of NF-κB and its DNA binding activity [272]. This plant is also used as antidiabetic in streptozotocin-induced diabetes mellitus mouse model [273].

164. Trachyspermum ammi: *T. ammi* is used for relieving kidney stone pains and urolithiasis. So far, its diuretic properties have been reported widely in literature and it is actively used in various drug formulations of kidney stone treatments. *Trachyspermum ammi* shown prevention in DMBA- and B(a)-P induced skin and forestomach papillomagenesis [274].

165. Tribulus terrestris: *Tribulus terrestris* had shown chemopreventive effect against 7,12- dimethylbenz (a) anthracene induced skin papillomagenesis in mice by oral gavage for 7 days [275]. It also showed protective effects in diabetes mellitus [276]. *In vivo* study suggested that methanolic and aqueous extracts of *T. terrestris* having antihypertensive and vasodilator effects [277].

166. Trigonella foenum-graecum: Diosgenin, a steroidal saponin present in fenugreek (*Trigonella foenum graecum*) and other plants, has been shown to suppress inflammation, inhibit proliferation, and induce apoptosis in a variety of tumor cells. It down-regulate TNF-induced expression of NF-κB-regulated gene products involved in cell proliferation (cyclin D1, COX-2, c-myc), antiapoptosis (IAP1, Bcl-2, Bcl-xL, Bfl-1/A1, TRAF1 and cFLIP), and invasion (MMP-9) [278]. It also inhibits STAT3 signaling pathway leading to suppression of proliferation and chemosensitization of human hepatocellular carcinoma cells [279]. 4-hydroxyisoleucine, an unusual amino acid isolated from Trigonella foenum-graecum seeds was characterized in type II diabetes [280].

167. Uraria lagopoides: It exhibits as antiviral compound and completely inhibits the growth of Reo virus [281]. Alcohol and aqueous extract of aerial parts of *Uraria lagopoides* showed anti-inflammatory activity in the rat paw edema test.

168. Valeriana officinalis: *Valeriana officinalis* (Valerianaceae) has been used for treating mild nervous tension and temporary sleeping problems. In traditional European medicine it has been also reported as an antiinflammatory remedy. Ethanolic extract of the underground parts of *V. officinalis* showed inhibitory activity against NF-κB on HeLa cells [282].

169. Valeriana wallichii: *V. wallichii* shown antidepressant effect, and used in gastrointestinal and cardiovascular disorders, as antispasmodic and hypotensive. This action is through K(ATP) channel activation [283]. It is also used in treating anxiety, tremors, inflammations of the joints, chorea, neurosis, and dysmenorrheal in Indian ayurveda.

170. Vanda roxburghii: Extract of *V. roxburghii* has wound-healing potential in rats. It augments the uterine contractions and is a bronchodilator, digestant and blood purifier. It is used in diseases like gout, rheumatic disorders, asthma, abdominal pain, fever and edema [284].

171. Vernonia cinerea: *V. cinerea* exhibits anti-cancer and anti-helmintic, anti-diuretic, anti-inflammatory, analgesic, anti-pyretic and anti-bacterial activities. Treatment of V. cinerea methanolic extract also showed an anti-inflammatory effect though enhancing phagocytic activity of peritoneal macrophages. Moreover the extract downregulated inflammatory mediators such as iNOS and COX-2, and decreased secretion of TNFa, IL-1β and IL-6 in LPS-treated macrophages [285].

172. Viola odorata: The leaf of this plant is used for treatment of tumor. Cyclotide from *V. odorata* showed cytotoxic effects against various drug-resistant tumor cells [286].

173. Vitex negundo: This plant showed anti-asthma, expectorant, antisepsis, hypoxia tolerance enhancement and also shown to could decrease blood glucose level. Vitexins have cytotoxic effect on various types of cancer cell lines and also have antitumor activity on tumor xenograft models including breast, prostate, liver, and cervical cancers [287].

174. Withania somnifera: The plant *Withania somnifera* Dunal (Ashwagandha), also known as Indian ginseng, is widely used in the Ayurvedic system of medicine to treat tumors, inflammation, arthritis, asthma, and hypertension. Chemical investigation of the roots and leaves of this plant has yielded bioactive withanolides. Withanolides suppressed NF-κB activation induced by a variety of inflammatory and carcinogenic agents; including TNF-α, IL-1β, doxorubicin, and cigarette smoke condensate. It also suppressed both inducible and constitutive NF-κB activation. The suppression occurred through the inhibition of inhibitory subunit of IκBα kinase activation, IκBα phosphorylation, IκBα degradation, p65 phosphorylation, and subsequent p65 nuclear translocation. Consequently, withanolide suppressed the expression of TNF-induced NF-κB-regulated gene products such as IAP-1, Bfl-1/A1, and FADD-like IL-1β-converting enzyme-inhibitory protein, COX-2 and ICAM-1, enhanced the apoptosis induced by TNF and chemotherapeutic agents, and suppressed cellular TNF-induced invasion and receptor activator of NF-κB ligand-induced osteoclastogenesis [288]. Withanolide sulfoxide is another active compound of this plant inhibits COX-2 expression [289]. Withaferin-A (WA) is a bioactive compound derived from *W. somnifera*, which showed ant-tumor activity through inhibition of Notch-1 signaling and down regulates prosurvival pathways, such as Akt/NF-κB/Bcl-2 [290].

175. Zingiber officinale: Traditionally, ginger has been used to treat a wide range of ailments including gastrointestinal disorders, such as stomachaches, abdominal spasm, nausea, and vomiting, as well as in arthritis and motion sickness. Phytochemical studies showed that the plant is rich in a large number of substances, including gingerols and shogaols. These compounds display diverse biological activities such as antioxidant, anti-inflammatory, and anticarcinogenic properties. They also exhibit a spasmolytic activity, which is mediated via blocking Ca^{2+} channels. A number of recent studies have renewed interest in ginger for the treatment of chronic inflammatory conditions [291].

Conclusions

Overall from this description, it is clear that reverse pharmacology approach to examine the plants for drug development is a viable approach. To fully validate this approach, further clinical trials are needed to examine their potential. It is anticipated that this approach will not be as expensive as currently used and the compounds/drugs isolated will be safe. Also

one must question why using a single chemical compound is preferred as a drug as compare to extracts from the whole plants. Benefits of a single chemical entity may be in convenience to understand its molecular mechanism. However, it may not be beneficial to the patient when examined, in part, due to the possibility of development of resistance to a single chemical entity. It is possible that when whole plant extract or combination of plant extracts are used, it may exhibit improved bioavailability and lower toxicity, as compared to single chemical entity.

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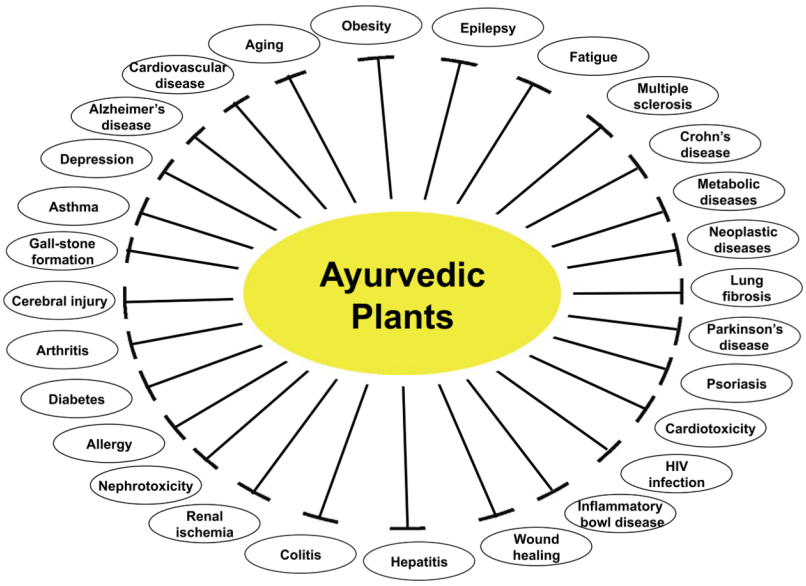

Fig. 1.
The use of Ayurvedic plants for treatment of various chronic diseases.

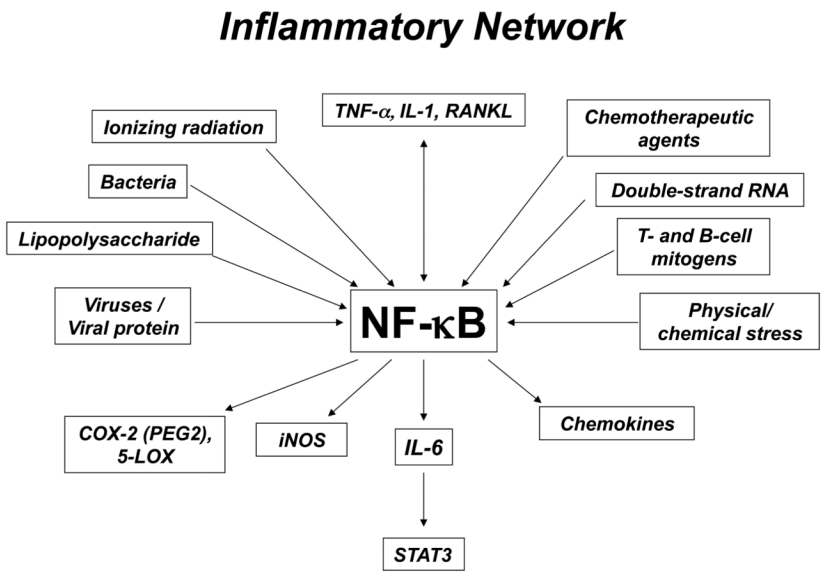

Fig. 2.
Activation of inflammatory network by various agents.

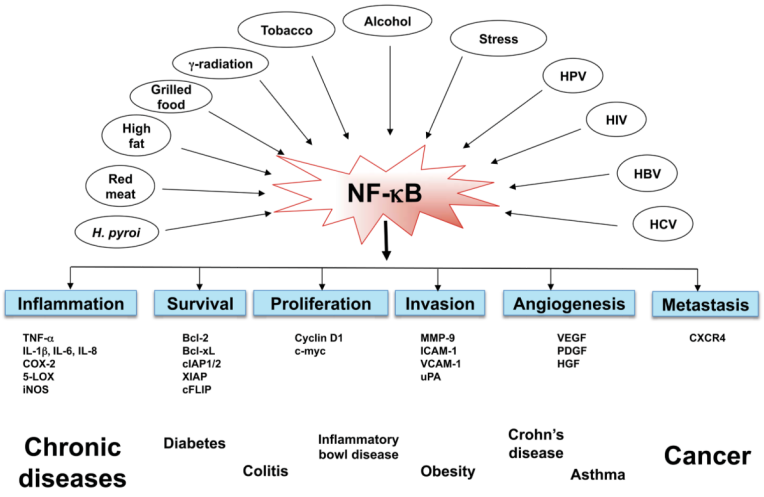

Fig. 3.

Activation of inflammatory network by life style factors and its contribution to chronic diseases.

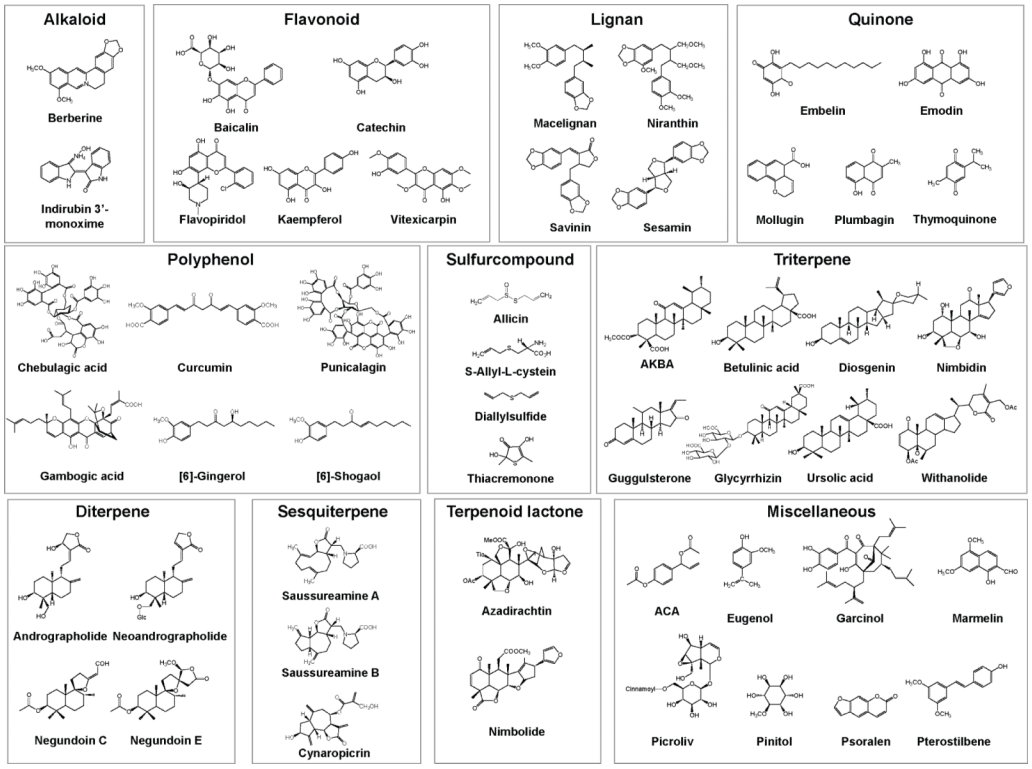

Fig. 4.
Structures of active phytochemicals derived from Ayurvedic plants.

Table 1

Ayurvedic formulations and their uses*

Formulation	Plants used	Uses
Amrutanjan Balm	*Cinnamomum camphora, C. zeylanicum, Cymbopogon citrates, Eucalyptus polybractea, Gaultheria sp., Mentha arvensis, M. piperita, Rosa sp., Thymus vulgaris*	Cures pain, sprain, cold and sinus
Ayurslim	***Commiphora wightii, Garcinia cambogia,*** *G. sylvestre,* ***Terminalia chebula, Trigonella foenum-graecum***	Burns fat and reduces cholesterol
Dabur Chyawanprash	*Phyllanthus emblica, Piper longum, Pistacia integerrima Pueraria tuberosa,* ***Tinospora cordifolia***	Protects from infections, coughs, cold and stress; adjuvant pulmonary tuberculosis therapy
Divya Arshkalpa Vati	***Aloe vera, Azadirachta indica, Berberis aristata****, C. camphora, Daemenorops draco, Sapindus sp.,* ***Solanum nigrum, T. chebula***	Cures piles, burning sensation and colic pain
Divya Ashmarihara Kvath	*Bergenia ligulata,* ***Boerhavia diffusa****, Crataeva nurvula Dolichos biflorus, Tribulus terrestris*	Diuretic, anti-oedemous; dissolves kidney, urinary & gall bladder stones
Divya Ashmarihara Rasa	*Hajarala yahuda, Hordeum vulgare, Raphanus sativus*	Diuretic, dissolves calculi, relieves pains, anti-oedemous.
Divya Danta Manjana	*Acacia arabica, Anacyclus pyrethrum,* ***A. indica****, C. camphora M. piperita, Mimusops elengi, P. longum, Quercus infectoria,* ***Syzygium aromaticum****, Zanthoxylum alatum*	Strengthens the gums and stops bleeding
Divya Gaisahara Choorna	*Citrus limon, Cuminum cymimum, Ferula foetida, Piper nigra,* ***T. chebula****, Trachyspermum ammi*	Reduces gas, acidity, flatulence, colic pain & anorexia
Divya Kayakalpa Kvatha	***Acacia catechu****,* ***A. indica****, B. aristata, Cassia tora, Cedrus deodara,* ***Curcuma longa****, Leucas cephalotes,* ***Picrorhiza kurroa****, Pongamia pinnata,* ***Psorlia corylifolia****,* ***Pterocarpus santalinus****,* ***Rubia cordifolia****, Swertia chirata* ***T. cordifolia***	Cures eczema, leprosy, filariasis; helps in reducing obesity
Divya Kayakalp Vati	***A. catechu****,* ***A. indica****, B. aristata, C. tora, C. deodara, Citrullus colocynthis,* ***C. longa****, Emblica officinalis, Leucas cephalotes,* ***Nigella sativa, P. kurroa****, Pongamia pinnata* ***P. santalinus, R. cordifolia****, Sarsa parilla, Solanum xantho-carpum, S. chirata, Terminalia belerica,* ***T. chebula, T. cordifolia***	Purifies blood, removes acne, pimples; cures from ring-worms, itches, pruritus, eczema, leucoderma & psoriasis
Divya Madhu-kalpa Vati	*Acacia arabica, Aconitum heterophilum,* ***Aegle marmelos, Andrographis paniculata****,* ***A. indica****,* ***C. longa****, C. zedoaria Emblica officinalis, Ficus bengalensis, G. sylvestre, Holarrhena antidysenterica, Momordica charantia,* ***N. sativa, P. kurroa,*** *S. chirata, Syzyium cumini, T. belerica,* ***T. chebula, T. cordifolia,*** *T. terrestris,* ***T. foenum-graecum, Withania somnifera***	Balance insulin secretion, strengthens immune system
Divya Medha Kwatha	*Bacopa monnieri, Celatrus paniculatus, Convovulus pluricaulis,* ***Foeniculum vulgare****, Lavandula stoechas, Nardostachys jatamansi, Onosma bracteatum,* ***W. somnifera***	Cures chronic headache, migraine, sleeplessness and depression
Divya Mukta Vati	*Acorus calamus, B. monnieri, C. paniculatus, C. pluricaulis, Inula racemosa, L. stoechas, N. jatamansi, Rauwolfia serpentina, T. arjuna,* ***W. somnifera***	Cures high blood pressure, insomnia, palpitation, chest pain
Divya Pidantaka Kvatha	*Cyperus rotundus, Nyctanthes arbortristis, Piper chaba, P. longum, Pluchea lanceolata, Ricinus communis, T. ammi,* ***Vitex negundo, W. somnifera, Z. officinale***	Useful in joint pain, sciatica, osteo-arthritis, gout, rheumatoid arthritis, muscular and skeletal pains and oedema.
Divya Udaramrita Vati	***A. marmelos****,* ***A. vera****,* ***B. diffusa****, E. officinalis, Mangifera indica, Operculina turpethum, Phyllanthus niruri,* ***P. kurroa****,* ***Plumbago zeylanica****,* ***S. nigrum****, T. belerica, T. ammi*	Cures jaundice, anaemia, chronic fever, diarrhoea and abdominal pain
Divya Yauvanamrita Vati	*Anacyclus pyrethrum, Asparagus racemosus, Castorium, Crocus sativus, Mucuna pruriens,* ***Myristica fragrans*** *Sida cordifolia*	Strengthens heart and brain, promotes luster and youthness and cures impotency.
Divya Udarakalpa Curna	*Cassia angustifolia,* ***F. vulgare, Glycyrrhiza glabra,*** *Rosa centifolia,* ***T. chebula***	Stimulates digestion and removes constipation
Divya Kayakalpa Taila	***A. indica****,* ***B. aristata****, C. tora, C. deodara,* ***C. longa****, E. officinalis, Leucas cephalotes,* ***N. sativa, P. kurroa****, P. pinnata,* ***Psorlia corylifolia****,* ***P. santalinus, R. cordifolia****, Saphindus trifoliatus, Sarsa parilla, Sesamum indicum, Solanum indicum, S. chirata,* ***T. chebula****,* ***T. cordifolia***	Cures skin diseases like ring worm, itching, sun burning, eczema, leucoderma, psoriasis, utricaria and skin allergy

Formulation	Plants used	Uses
Divya Kesa Taila	*Abrus precatorius, B. monnieri,* ***B. aristata***, ***Callicarpa macrophylla,*** *C. rotundus, Eclipta alba, E. officinalis, Fagonia cretica,* ***Indigofera tinctoria****, Mesua ferrea, N. jatamansi,* ***Nelumbo nucifera****, Onosma ehioides, Pandanus tectorius,* ***P. santalinus****, S. cordifolia, Symplocos crataegoides*	Cures untimely hair fall, dandruff, alopecia, premature graying of hair
Divya Churna	***F. vulgare,*** *Ipomoea nil, R. centifolia,* ***T. chebula****,* ***Z. officinale***	Cures abdominal pain, flatulence, heaviness & nausea
Divya Peya (Herbal Tea)	*Adhatoda vasia, B. monnieri,* ***B. diffusa****, C. zeylanicum, C.*	Controls cholesterol and protects from heart diseases;
	pluricaulis, Cymbopogon martini, C. rotundus, Elettaria cardamomum, Ephedra gerardiana, ***F. vulgare, M. fragrans, Nelumbo nucifera****,* ***Ocimum sanctum****, P. niruri, P. chaba, P. longum, P. nigrum,* ***P. zeylanica****,* ***P. santalinus****, R. centifolia, Santalum album,* ***S. aromaticum****, T. arjuna,* ***T. cordifolia,*** *Viola odorata, W****. somnifera, Z. officinale***	promotes immunity, stimulates digestion
Divya Dhara	*C. camphora, M. piperita,* ***S. aromaticum****, T. ammi*	Cures asthma, cholera, ear-diseases, epitaxis, trauma, utricaria, cough, colic pain and flatulence
Divya Pidantaka Rasa	***A. marmelos****, Clerodendron phlomoides,* ***Commiphora mukul,*** *C. rotundus, Gmelina arborea, Moringa oleifera, Oroxylum indicum, P. lanceolata, Pseudarthria viscida, S. indicum, Stereospermum suaveolen, Strychnos nuxvomica* ***T. cordifolia****, T. ammi, T. terrestris, Uraria lagopoides,* ***V. negundo, W. somnifera***	Useful in joint pain, arthritis, lumbar pain, cervical spondylitis and sciatica
Divya Pidantaka Taila	*Aconitum ferox, A. calamus,* ***A. marmelos****,* ***Allium sativum****, Anethum sowa, A. racemosus,* ***B. aristata****, Butea mono-sperma, Calotropis procera, C. paniculatus, C. zeylanicum, C. phlomoides,* ***C. longa****, Datura metel, E. alba,* ***F. vulgare****,* ***G. glabra,*** *G. arborea, Hebenaria intermedia, I. racemosa, Lilium polyphyllum, Malaxis acuminate, M. ferrea, N. jatamansi, Oroxylum indicum, Paderia foetida, P. chaba, P. longum, P. lanceolata,* ***P. zeylanica****, Polygonatum verticillatum, Pseudarthria viscida, R. communis, Roscoea alpina,* ***R. cordifolia****, Sesamum indicum, S. indicum, Stereospermum suaveolen, Strychnos nuxvomica, T. ammi, T. terrestris, Uraria lagopoides, Valeriana wallichii,* ***V. negundo, Z. officinale***	Relieves pain of lumbar region, knee-joints, cervical spondylitis, oedema & inflammation
Divya Madhunasini Vati	*A. arabica, A. heterophilum,* ***A. marmelos****,* ***A. paniculata****,* ***A. indica, C. longa,*** *C. zedoaria, E. officinalis, F. bengalensis, G. sylvestre, Holarrhena antidysenterica, M. charantia, N.* ***sativa****,* ***P. kurroa****, S. chirata, Syzyium cumini, T. belerica,* ***T. chebula, T. cordifolia,*** *T. terrestris,* ***T. foenum-graecum, W. somnifera***	Balance insulin secretion, strengthens immune system
Divya Medha Vati	*A. calamus, B. monnieri, C. paniculatus, C. pluricaulis, I. racemosa, Lavandula stoechas, N. jatamansi,* ***W. somnifera***	Cures mental disorders, depression and epileptic fits
Divya Amirta Rasayana	*A. racemosus, B. monnieri, Bambusa arundinacea, C. zeylanicum, C. pluricaulis, C. sativus, E. cardamomum, E. officinalis, M. prurita, Prunus amygdalus*	Rejuvenates and nourishes the brain and body
Divya Medohara Vati	***B. diffusa, C. mukul,*** *E. officinalis,* ***E. ribes****, Operculina turpethum,* ***P. kurroa****, T. belerica,* ***T. chebula***	Thyroid disorders, rheumatic arthritis, joint pains, pain to lumbar region and knee joints.
Divya Svasari Rasa	*A. feroz, Anacyclus pyrethrum, Capparis moonii, C. zeylanicum,* ***G. glabra****, P. longum, P. nigrum, Pistacia integerrima,* ***S. aromaticum****,* ***Z. officinale***	Bronchitis, cough, coryza, cold, asthma and sinusitis
Divya Strirasayana Vati	*A. racemosus, Bambusa arundinacea,* ***B. aristata****, Bryonia laciniosa, C. deodara,* ***C. mukul****, E. officinalis,* ***G. glabra****, M. ferrea,* ***N. nucifera****, Putranjiva roxburghii, S. album, Saraca asoca, S. cordifolia, T. belerica,* ***T. chebula****,* ***W. somnifera***	Leucorrhoea, menorrhagia, irregularity in menstruation
Divya Hridayamrita Vati	***B. diffusa, C. mukul,*** *C. rotundus, P. lanceolatus,* ***P. zeylanica*** *T. arjuna,* ***T. cordifolia****,* ***V. negundo***	Removes the arterial block, angina pain and palpitation
Divya Silajita Rasayana Vati	*E. officinalis, P. niruri, T. belerica,* ***T. chebula, W. somnifera***	Diabetes & leucorrhoea
Divya Sarvakalpa Kvatha	***B. diffusa****, Cassia fistula, P. niruri,* ***S. nigrum***	Cures jaundice, oedema, oliguria, oedema

Formulation	Plants used	Uses
Divya Kanti Lepa	***A. catechu***, *C. camphora, Curcuma amada,* ***C. longa***, ***M. fragrans,*** ***R. cordifolia***, *S. album, Valeriana wallichii*	Cures skin disorders viz pimples, acne, wrinkles on face
Divya Vatari Churna	*M. oleifera,* ***P. kurroa, T. foenum-graecum, W. somnifera***, ***Z. officinale***	Cures rheumatoid arthritis, sciatica, pain in back and lumbar region
Himalaya Abana	*A. calamus, A. racemosus,* ***B. diffusa***, *C. copticum, Celastrus paniculatus, Centella asiatica, Cinnamomum cassia,* ***C. wightii,*** *C. pluricaulis, C. sativus, C. rotundus, E. alba, E. cardamomum,* ***E. ribes***, *E. officinalis,* ***F. vulgare***, ***G. glabra***, *N. jatamansi, Nepeta hindostana,* ***O. sanctum***, *P. longum, Rosa damascena, R. centifolia, S. album****,*** ***S. aromaticum,*** *T. arjuna,* ***T. chebula, T. cordifolia, W. somnifera, Z. officinale***	Hyperlipidemia and hypertension, adjuvant in angina therapy
Himalaya Cystone	*Achyranthes aspera, Cyperus scariosus, Didymocarpus pedicellata, Onosma bracteatum,* ***R. cordifolia***, *Saxifraga ligulata, Vernonia cinerea*	Prevents urinary infections & stone formation
Himalaya Dental Cream	*A. arabica,* ***A. catechu***, *A. farnesiana, Pistacia, C. copticum* ***E. ribes***, *E. officinalis, Mimusops elengi,* ***Punica granatum*** *Salvadora persica, T. bellerica,* ***T. chebula***, *V. negundo, Zanthoxylum alatum*	Stops gum bleeding, boils and sores
Himalaya Diabecon	*Abutilon indicum,* ***A. vera***, *A. racemosus****,*** ***B. aristata***, ***B. diffusa,*** *Casearia esculenta,* ***C. wightii, C. longa***, *Eugenia jambolana,* ***G. glabra***, *G. arborea, Gossypium herbaceum G. sylvestre, M. charantia,* ***O. sanctum***, ***Phyllanthus amarus***, *P. nigrum****,*** ***Pterocarpus marsupium***, *Rumex maritimus, Sphaeranthus indicus, S. chirata,* ***T. cordifolia***, *T. terrestris,* Trikatu, Triphala	Reduce blood sugar levels and diabetic complications
Himalyaya Geriforte	*Achillea millefolium, Argyeria speciosa, Asparagus adscendens, A. racemosus,* ***B. aristata***, *Caesalpinia digyna, Capparis spinosa, C. copticum, Cassia occidentalis, Centella asiatica, Cichorium intybus, C. sativus****,*** ***C. longa,*** *E. alba, E. cardamomum,* ***G. glabra***, *M. pruriens,* ***M. fragrans***, *P. longum,* ***S. aromaticum***, *Tamarix gallica, T. arjuna,* ***T. chebula***	Slows down aging, reduces stress and enhances immunity
Himalaya Himplasia	***A. catechu,*** *A. racemosus, Caesalpinia bonducella, Tribulus terrestris*	Inhibits prostatic stromal proliferation & improves fertility
Himalaya Liv52	*A. millefolium, C. spinosa, C. occidentalis, Cichorium intybus,* ***S. nigrum***, *Tamarix gallica, T. arjuna*	Pre- and early cirrhosis, viral hepatitis & alcoholic liver disease
Himalaya Menosan	*A. racemosa, Centella asiatica,* ***G. glabra***, *Saraca indica S. cordifolia,* ***T. chebula***	Regulates overall hormonal balance & urinary tract function
Himalaya Mentat	*A. calamus, B. monnieri, C. paniculatus, C. asiatica,* ***E. ribes***, *E. cardamomum, E. officinalis, Evolvulus alsinoides,* ***F. vulgare***, *Ipomoea digitata, M. pruriens,* ***M. fragrans***, *N. jatamansi, Orchis mascula, Oroxylum indicum, P. amygdalus,* ***S. aromaticum,*** *T. arjuna, T. bellirica,* ***T. chebula***, ***T. cordifolia,*** *Valeriana sp.* ***W. somnifera, Z. officinale***	Adjuvant in Parkinson's and Alzheimers diseases
Himalaya Pilex	*Bauhinia variegata,* ***B. aristata***, *C. fistula,* ***C. wightii***, *E. officinalis,* ***Melia azadirachta***, *M. ferrea, T. bellirica,* ***T. chebula***	Treats piles, cures hemorrhoids, treats varicose veins
Himalaya Purim	***A. paniculata***, *Pistacia, C. fistula, Crataeva magna,* ***C. longa***, *E. alba,* ***E. ribes***, *E. officinalis,* ***P. kurroa***, ***Psoralea corylifolia***, ***Saussurea lappa***, *T. bellerica,* ***T. chebula***, ***T. cordifolia***	Regulates detoxification and cleansing
Himalaya Reosto	***C. wightii***, *Sida cordifolia, T. arjuna, Vanda roxburghii,* ***W. somnifera***	Reverses hypogonadism and osteoporosis
Himalaya Rumalaya Forte	***Alpinia galanga***, ***Boswellia serrata***, ***C. wightii, G. glabra T. cordifolia***, *Tribulus terrestris*	Relieves pain from arthritis and traumatic inflammation
Rumalaya Gel	***B. serrata***, *Cedrus deodara, Cinnamomum zeylanicum Gaultheria fragrantissima, M. arvensis, Pinus roxburghii* ***V. negundo, Z. officinale***	Analgesic, relieves pain, joint mobility
Himalaya Septilin	***C. mukul,*** *E. officinalis,* ***G. glabra***, *Moringa pterygosperma* ***R. cordifolia***, ***T. cordifolia***	Strengthens immune system & body's defense mechanisms
Himalaya Triphala	*E. officinalis, T. bellrica,* ***T. chebula***	Reduces high blood pressure and hyper tension; effective in irritable bowel syndrome, ulcerative colitis and tumor

Boldface indicates anti-inflammatory activity shown in Table 4.

*The information is derived from websites http://www.divyayoga.com, http://www.himalayahealthcare.com, and http://amrutanjan.com, to illustrate as examples of Ayurvedic formulations, with no connection or affiliations to them of the authors.

Table 2

A list of Ayurvedic plants, their active components and their role in chronic diseases

Plant	Active compounds	In-vitro	In-vivo	Review
Abrus precatorius	Abruquinones	[243]	[11]	
	Abrin	[244]	[245]	
	Abrus agglutinin	[246]	[246]	
	ABP		[247]	
Abutilon indicum	Extract		[12]	
Acacia arabica	Gum	[248]		
Acacia catechu	Flavocoxid	[14]	[249]	
Acacia farnesiana	Acasiane, Farnesirane	[15]		
Achillea millefolium	Casticin	[250]		[251]
	Extract		[252]	
Achyranthes aspera	Extract		[17, 18, 253]	
Acorus calamus	Extract	[20]	[21, 254]	
Adhatoda vasica	Extract		[255, 256]	[257]
	Ambroxol	[22]		
Aegle marmelos	Marmelin	[25]		[258]
	Extract		[259]	
Allium sativum	Thiacremonone	[29]		
	1,2-vinyldithiin	[30]		[260–263]
	Diallyl sulfide/trisulfide	[264, 265]		
	Allicin	[266, 267]		
	Extract		[26, 27]	
Aloe vera	Aloe-emodin	[268, 269]		[270]
	Extract		[271, 272]	[273, 274]
Alpinia galanga	Acetoxychavicol acetate	[275–277]		
Andrographis paniculata	Andrographolide	[278–285]	[286–290]	
	Neoandrographolide	[291]		
	Andrograpanin	[292, 293]		
	Extract		[294, 295]	
	Composition		[296, 297]	
Areca catechu	Extract	[39, 298]		
Argyeria speciosa	Extract		[17, 299–302]	
Asparagus adscendens	Extract	[40]	[303]	
Asparagus racemosus	Extract	[304]	[41, 305, 306]	[307, 308]
Azadirachta indica	Azadirachtin/	[43, 309]		[310–312]
	Nimbolide	[42, 313]		
	Extract	[314]	[312, 315–320]	
Bacopa monnieri	Bacoside-A		[44, 45]	
	Triterpene saponins		[321]	
	Extract	[322]	[323, 324]	

Plant	Active compounds	In-vitro	In-vivo	Review
Bambusa arundinacea	Extract		[46]	
Bauhinia variegata	Extract	[47, 48]	[325–327]	
	Flavonoids	[328]		
Berberis aristata	Berberine	[50]	[329, 330]	
Bergenia ligulata	Extract	[331]		
Boerhaavia diffusa	Extract	[332–335]	[334, 336–339]	
	Punarnavine		[340, 341]	
	Flavonoids	[342]		
Boswellia serrata	AKBA	[61, 343–345]	[54–56, 58–60, 346–348]	
Bryonia laciniosa	Extract		[62]	
Butea monosperma	Butrin/isobutrin/butein	[349]		
	Stigmosterol		[350]	
	Extract	[351]	[352–357]	
Caesalpinia bonducella	Oil/Extract		[358–360]	
Caesalpinia digyna	Extract		[64]	
Calotropis procera	Latex extract	[361]	[362–365]	
Capparis spinosa	Extract	[68, 366]		
Carum copticum	Extract		[367–369]	
Casearia esculenta	3-hydroxymethyl xylitol		[370]	
	Extract		[371]	
Cassia angustifolia	Exract		[71]	
Cassia fistula	Extract		[72, 372–374]	
Cassia occidentalis	Extract	[375]	[73, 376, 377]	[378]
Cassia tora	Ononitol monohydrate		[379]	
	Extract	[380]	[381–383]	
Cedrus deodara	Extract/oil	[384]	[75, 385]	
Celastrus paniculatus	Extract	[386]	[76, 387]	
Cichorium intybus	Magnolialide	[388]		
	Cichotyboside		[389]	
	Extract		[77, 390, 391]	
Cinnamomum camphora	Extract	[79]	[247]	
Cinnamomum cassia	Extract	[392]	[80, 393, 394]	[395]
	Cinnamaldehyde	[396–398]		
Cinnnamomum zeylanicum	Extract	[399–401]	[402, 403]	
	Oil		[81]	
Citrullus colocynthis	Extract		[404–407]	
Commiphora mukul	Guggulsterone	[408–410]	[411–416]	[417–419]
	Gugulipid		[420, 421]	
	BHUx		[422]	
Commiphora wightii	Extract	[423, 424]		
Convolvulus pluricaulis	Extract		[425–427]	
Crocus sativus	Safranal, Crocin	[428]	[429–432]	[433–435]

Plant	Active compounds	In-vitro	In-vivo	Review
	Extract	[436, 437]	[438, 439]	
Cuminum cymimum	Extract/oil		[91, 440–444]	
Curcuma amada	Extract		[92]	[445]
Curcuma longa	Curcumin	[93–95]	[446–449]	[450–464]
Curcuma zedoaria	Curdione	[465, 466]		[96]
	Extract	[467–469]	[470, 471]	
Cymbopogon citratus	Citral	[472, 473]		
	Extract/oil	[98, 474]	[97, 475–477]	
Cyperus rotundus	Extract	[478, 479]	[480]	
Cyperus scariosus	Extract		[101]	
Didymocarpus pedicellata	Extract	[104]		
Dolichos biflorus	Extract		[481, 482]	
Eclipta alba	Extract		[483–487]	
Elettaria cardamomum	Extract	[110]	[109, 488–490]	
Embelia ribes	Embelin	[491]	[492–495]	
	Extract		[496–498]	
Emblica officinalis	Pyrogallol	[499]	[500]	
	Extract		[20, 501–504]	
Eugenia jambolana	Extract	[505]	[506–510]	
Evolvulus alsinoides	Extract		[511–513]	
Fagonia cretica	Extract		[116]	
Ferula assafoetida	Gum/Extract	[514]	[515–517]	
Ficus bengalensis	Leucodelphinidin	[518]		
	Extract		[118, 519–522]	
Foeniculum vulgare	Anethole	[120]	[523]	
	Extract	[524]	[523, 525–528]	
Garcinia cambogia	Garcinol	[529–531]	[532]	[533]
	Extract		[121, 534, 535]	
Glycyrrhiza glabra	Isoliquiritigenin	[536]		
	Glycyrrhizin		[537]	
	Glabridin	[538]	[538]	
	Extract	[539–541]	[126, 540, 542]	
Gymnema sylvestre	Extract		[543–545]	[546, 547]
Hemidesmus indicus	HMBA	[548]	[549, 550]	
	Extract		[551]	
Holarrhena antidysenterica	Extract		[552]	
Hordeum vulgare	Extract	[134, 553]	[554]	
Indigofera tinctoria	TCA		[555]	
	Indigtone		[556]	
	Extract		[557, 558]	
Inula racemosa	Extract	[559]	[136, 543, 560]	
Ipomoea nil	Extract	[561]		

Plant	Active compounds	In-vitro	In-vivo	Review
Lavendula stoechas	Extract	[562, 563]		
Leucas cephalotes	Extract		[140]	
Mangifera indica	Extract	[564–567]	[565, 568–573]	
	3beta-taraxerol	[574]		
	Mangiferin		[575]	
Mentha piperita	Extract	[576]	[577, 578]	[579]
	Oil	[580, 581]		
	Flavonoid		[582]	
Mimusops elengi	Extract		[147, 583]	
Momordica charantia	Extract	[584–588]	[589–594]	[148, 595]
Moringa oleifera	Extract		[596–601]	[602]
Mucuna pruriens	Extract		[603–607]	
Nardostachys jatamansi	Extract		[608–611]	
Nelumbo nucifera	(S)-armepavine		[154, 612, 613]	[614]
	Neferine		[615]	
	Kaempferol	[616]		
	Isoliensinine	[617]		
	Extract		[618–620]	
Nigella sativa	Thymoquinone	[621]	[621–628]	[629–631]
	Polyphenols		[632]	
	Extract	[633]	[624, 634–637]	
Nyctanthes arbortristis	arbortristoside-A		[156]	
	Extract		[638, 639]	
Ocimum sanctum	Eugenol		[640, 641]	[642, 643]
	Extract/oil	[644]	[320, 645–647]	
Operculina turpethum	Extract		[161, 648]	
Orchis mascula	Extract		[162]	
Oroxylum indicum	Baicalein	[163]		
	Extract	[649, 650]	[651]	
Phyllanthus amarus	Niranthin		[165]	
	Phyllanthin	[652]		
	Extract/lignan		[653–659]	
Phyllanthus niruri	Arabinogalactan	[660]		[661]
	Extract/lignan	[662]	[662–666]	
Picrorhiza kurroa	Picroliv		[667–670]	[671]
	Extract	[166, 672]		
Piper chaba	Amides/Extracts		[673, 674]	
Piper longum	Piperine	[675]	[675–677]	
	Piperlongumine	[678]		
	Piperinic acid	[679]	[679, 680]	
	Extract/oil	[167]	[681–684]	
Piper nigrum	Piperine		[685–687]	[688, 689]

Plant	Active compounds	In-vitro	In-vivo	Review
	Extract	[110]	[690]	
Pistacia integerrima	Extract		[169, 691]	
Pluchea lanceolata	Extract		[692, 693]	
Plumbago zeylanica	Plumbagin	[172, 694, 695]	[664, 696]	
	Seselin	[697]		
	Suberosin	[698]		
Pongamia pinnata	Pongamol, Karanjin		[699]	
	Extract		[700–704]	
Psoralea corylifolia	Bavachin	[705]		
	Psoralen		[706]	
	Bakuchiol	[707, 708]		
	Furocoumarins		[709]	
	Extract	[710, 711]	[710, 712]	
Pterocarpus marsupium	Pterostilbene		[179]	
	Flavanoids		[713]	
	Extract		[714]	
Pterocarpus santalinus	Savinin	[715]		
	Extract		[180, 716]	
Pueraria tuberaosa	Lupinoside		[717]	
	Extract		[718]	
Punica granatum	Ellagitannins		[181, 719]	[720–722]
	Punicalagin	[723]	[181, 723]	
	Anthocyanin		[724]	
	Extract	[725, 726]	[727–729]	
Putranjiva roxburghii	Extract		[182]	
Quercus infectoria	Extract		[183, 730]	
Raphanus sativus	Extract	[731]	[732, 733]	[734]
Ricinus communis	Ricinoleic acid		[188]	
	Extract		[735–737]	
Rosa damascena	Flavonoids	[190]		
	Extract/oil		[738–740]	
Rubia cordifolia	Rubiadin		[741]	
	Mollugin	[191]		
	Extract		[742–744]	
Rumex maritimus	Extract		[745]	
Salvadora persica	Extract		[193]	
Santalum album	Oil		[746]	
	Lignan	[747]		
Saphindus trifoliatus	Extract		[196, 748]	
Saraca indica	Saracin	[198]		
Saussurea lappa	Extract	[749]	[17]	
	Lactone	[750]		

Plant	Active compounds	In-vitro	In-vivo	Review
	Arctigenin	[751]		
	Cynaropicrin	[752, 753]		
	Costunolide	[754]		
Sesamum indicum	Sesaminol		[755, 756]	
	Sesamin	[201]		
	Sesamol		[757]	
	Extract		[758–761]	
Sida cordfolia	Extract		[762–766]	
Solanum indicum	Extract	[767]	[203]	
Solanum nigrum	Extract	[768, 769]	[748, 755, 770–773]	
Solanum xanthocarpum	Extract		[206, 774]	
Sphaeranthus indicus	7-hydroxyfrullanolide	[775]		
	Extract		[207, 776]	
Stereospermum suaveolen	Extract		[208, 777]	
Strychnos nuxvomica	Brucine	[209]	[778]	
	Extract	[779, 780]		
Swertia chirata	Amarogentin		[210]	
	Extract		[781, 782]	
Symplocos crataegoides	Triterpenes	[211]		
Syzygium aromaticum	Acetyl eugenol	[783]		
	Extract		[212, 784, 785]	[786]
Syzyium cumini	ferulic acid		[787] [788]	
	Extract		[789–792]	
Tamarix gallica	Extract		[214, 793]	
Terminalia arjuna	Arjunic acid		[794]	
	Casuarinin	[795, 796]		
	Terminoside A	[797]		
	Extract		[215, 216, 798–800]	[801]
Terminalia belerica	Extract		[549, 802–806]	
Terminalia chebula	Chebulagic acid	[807]	[808]	
	Extract		[549, 803, 806, 809–812]	
Thymus vulgaris	Thymol, Carvacrol	[813]		
	Extract	[220]	[814]	
Tinospora cordifolia	Extract	[815]	[222, 506, 816–819]	
Trachyspermum ammi	Extract		[225, 820]	
Tribulus terrestris	Tribulosin		[821]	
	Saponion	[822]	[823]	
	Extract		[226, 228, 824, 825]	
Trigonella foenum-graecum	Diosgenin	[826]	[229, 826, 827]	
	Galactomannan		[828]	
	Extract		[829–836]	
Valeriana wallichii	Extract		[837, 838]	

Plant	Active compounds	In-vitro	In-vivo	Review
Vanda roxburghii	Extract		[235, 839]	
Vernonia cinerea	Extract	[236]	[757, 840–843]	
Viola odorata	Cycloviolacin	[844]		
	Extract	[845]		
Vitex negundo	Vitexins		[238]	
	Diterpenes	[846]		
	Extract		[847–850]	
Withania somnifera	Withaferin-A	[851, 852]	[241]	[853]
	Withanolide sulfoxide	[240]	[854]	
	Withanamides	[855]		
	Extract	[856]	[857–859]	
Zingiber officinale	[6]-Gingerol	[860]	[860, 861]	
	6-Shogaol	[862–864]		
	Extract	[865, 866]	[867–871]	[872, 873]

ABP, abrin-derived peptide; AKBA, Acetyl-11-keto-β-boswellic acid; TCA, trans-tetracos-15-enoic acid; HMBA, 2-hydroxy-4-methoxy benzoic acid

Table 3

List of inflammatory gene products regulated by NF-κB*

Enzymes	Stress response genes	Gro b	CD21	Lox-1	Clone 330
11bHSD2	12-LOX	Gro g	CD38	Ly49	Clone 68
17bHSD	5-LOX	Gro-1	CD3g	Mdr1	Connexin32
ABC Transporters	COX-2	ICOS	CD40	mGlu2	Cyclin D1
ADH	Cu/Zn SOD	IFN-g	CD48	Mu-OR	Cyclin D2
AID	CYP2C11	IiGp1	CD83	NMDA-RS 2A	Cyclin D3
alpha 1ACT	CYP2E1	IL-1 RA	CD86	NP Y-Y1 R	DIF2
AMACR	CYP7b	IL-10	CD98	NR-1	DMT1
ARFRP1	FHC	IL-11	CXCR	Oxytocin R	Elafin
ASS	GCL	IL-12A	CXCR2	PAF-R1	Endothelin 1
Aromatase	GCLM	IL-12B	F11-R	P-gp	Ephrin-A1
ART2.1	HSP90-a	IL-13	Fc e R II	RAGE	epsilon-Globin
BACE-1	iNOS	IL-15	FcRn	**Transcription factors**	Factor VIII
Btk	MAP4K1	IL-17	HLA-G	**/Regulators**	FHC
Cathepsin B	Mx1	IL-1a	ICOS	A20	Gadd45b
Cathepsin L	DTD	IL-1b	Ig C g1	ABIN-3	Galectin 3
cdk6	cPLA2	IL-2	Ig e heavy chain	AR	Galpha i2
CGT	SENP2	IL-23A	Ig g1	Bcl-3	GBP-1
CHI3L1	SEPS1	IL-27	Ig g4	BMI-1	GIF
CRAD1	SOD1	IL-6	Ig k light chain	C/EBPd	Gro-1
CRAD2	SOD2	IL-8	IL-2 R a-chain	CDX1	GS3686
Collagenase 1	**Early response genes**	IL-9	Invariant Chain II	c-fos	HK protein
DDH	B94	IP-10	Kinin B1 Receptor	c-myb	HCCS1
DNASIL2	Egr-1	KC	MHC-I (H-2Kb)	c-myc	HMG14
DYPD	p22/PRG1	LIX	MHC-I HLA-B7	c-rel	IBABP
EL	p62	Lymphotoxin a	Nod2	DC-SCRIPT	IMP2
ENO2	TIEG	Lymphotoxin b	PGRP-S	Dmp1	K15 Keratin
gamma-GCS	**Viruses**	MCP-1/JE	Polymeric Ig R	E2F3a	K3 Keratin
GAD67	AV	MIG	T-CR b chain	Elf3	K6b Keratin
GCL	AVV	MIP-1a,b	T-CR/CD3g	ELYS	Lactoferrin

Enzymes	Stress response genes	Gro b	CD21	Lox-1	Clone 330
GCLM	BLV	MIP-2	TLR-2	ETR101	Laminin-B2
GCLC	CMV	MIP-3a/CCL20	TLR9	Gata-3	Lipocalin-2
GD3-synthase	EBV	mob-1	TNF-Receptor	GCR	MCT1
Gelatinase B	HBV	NAP-78	TREM-1	HIF-1a	Mir125b
G6PD	HIV-1	RANTES	b-2 Microglobulin	HOXA9	Mir146a, b
Glc-6-Pase	HPV-16	T-CA gene 3	**Growth factors/ligands**	IkB-a	Mir155
GnRH II	HSV	TNFalpha	Activin A	IkB-e	MNE1
gp91 phox	JCV	TNFbeta	Angiopoietin	IRF-1	Mts1
Granzyme B	SIV	TRAIL	BCAP	IRF-2	Mucin
GSTP1-1	SV-40	Treefoil factor-3	BDNF	IRF-4	MBP
H+-K+ATPase a2	**Apoptosis Regulators**	VEGI	BLNK	IRF-7	Naf1
Heparanase	ASC	**Cell adhesion molecules**	BLyS	jmjD3	NGL
HO-1	B7-H1	CD44	BMP-2	junB	NLF1
Has	Bax	DC-SIGN	BMP-4	Lef1	p11
IDO	Bcl-2	ELAM-1	CGRP	LZIP	p21-CIP1
iNOS	Bcl-xL	Endoglin	EPO	Mail	PA28 a
ITD-2	Bfl1/A1	Fibronectin	FGF8	nfkb1	PA28 b
L-PGDS	Bim	ICAM-1	FLRG	nfkb2	PAI-1
Lysozyme	BNIP3	MadCAM-1	G-CSF	NLRP2	Pax8
MMP-3	Caspase-11	NCAM	GM-CSF	NURR1	PCBD
MMp-9	CD95 (Fas)	P-selectin	HGF/SF	Osterix	Perforin
MKP-1	c-FLIP	Tenascin-C	IGFBP-1	p53	PGK1
MLCK	CIDEA	VCAM-1	IGFBP-2	PR	POMC
Mthfr	FAPase-1	**Acute phase proteins**	M-CSF	PU.1	PSG
GnT-I	Fas-Ligand	Angiotensinogen	Midkine	relb	PDYN
n-NOS	IAPs	b-defensin-2	NGF	Snail	PSA
PDE7A1	IEX-1L	C4b BP	NK-1R	Sox9	PTEN
PGES	Nr13	CF-κB	NK4	Stat5a	RAG-1
PIK3CA	TRAF-1	CF-C4	Nrg1	Tfec	RAG-2
PIM-1	TRAF-2	C-RP	OPN	Twist	RbAp48
PKAalpha	TRAF-2 BP	Hepcidin	PDGF B chain	WT1	RICK

Enzymes	Stress response genes	Gro b	CD21	Lox-1	Clone 330
PKCdelta	XIAP	LPS BP	PlGF	YY1	S100A6
PLCdelta	**Cytokines/Chemokines**	Pentraxin-3	Proenkephalin	**Miscellaneous**	SerpinE2
Plk3	aka (LAG-1)	SAA1	Prolactin	AGP	SH3BGRL
PP5	BAFF	SAA2	SCF	a1-AT	SK2 channels
PTGIS	b-Interferon	SAA3	THBS1	a2(I) collagen	Skp2
PTHrP	BLIMP-1	Tissue factor-1	THBS2	ABCG5	Spergen-1
PTP1B	CCL15	UPA	VEGF C	ABCG8	SWS1
RACK1	CCL17	**Antigen presentation**	WNT10B	AbetaH-J-J	Syncytin-1
REV3	CCL19	Complement B	**Cell-surface receptors**	AFP	Syndecan-4
Serpin 2A	CCL20	Complement component 3	A1 AR	AMH	TASK-2
SIAT1	CCL22	Complement Receptor 2	A2A	APOBEC2	TAUT
Slfn-2	CCL23	Peptide Transporter TAP1	a2B-AR	Apo CIII	TFPI-2
SNARK	CCL28	Proteasome Subunit LMP2	ABCA1	Apo D	Transferrin
sGC-1	CCL5	Tapasin	ABCC6	Apol E	TRIF
SSAT	CINC-1	**Immunoreceptors**	ADAM19	AQP4	TRPC1
SUV3	CXCL 11	B7.1 (CD80)	AS Na-channel	b-amyloid	UBE2M
TERT	CXCL5	BRL-1	Bradykinin B1-R	Biglycan	UCP-2
TG	CXCL6	CCR5	CD23	BRCA2	Uroplakin Ib
TTG	EBI3/IL-27B	CCR7	CD69	Calsarcin-1	Vimentin
type II-sPLA(2)	Eotaxin	CD134	DOR	Caveolin-1	zeta-Globin
		CD137	EGFR	Claudin-2	
UPase	Fractalkine	CD154	ErbB2	Clone 156	
XDH	Gro a		Gal1 R		

*Adopted from www.nf-kb.org

Table 4

Selected Ayurvedic Plants, Their Phytochemicals and Their Molecular Targets

Ayurvedic Plants Alkaloid	Active Compounds	Molecular Targets	References
Berberis aristata	Berberine	NF-κB, COX-2	[50]
Indigofera tinctoria	Indirubin	NF-κB, COX-2	[135]
Flavonoid			
Acacia catechu	Baicalin, catechin	COX-2, 5-LOX, iNOS	[14]
Dysoxylum binectariferum	Flavopiridol	NF-κB, COX-2	[107]
Nelumbo nucifera	Kaempferol	NF-κB, COX-2, iNOS	[155]
Lignan			
Myristica fragrans	Macelignan	NF-κB, COX-2	[874, 875]
Phyllanthus amarus	Niranthin	PAFR	[165]
Pterocarpus santalinus	Savinin	TNF-α	[715]
Quinone			
Embelia ribes	Embelin	NF-κB, COX-2	[112]
Aloe vera	Emodin, lectin	NF-κB, TNF-α	[32, 876]
Rubia cordifolia	Mollugin	NF-κB	[191]
Plumbago zeylanica	Plumbagin	NF-κB, COX-2, STAT-3	[172, 173]
Nigella sativa	Thymoquinone	NF-κB, TNF-α, IL-1β, COX-2	[8, 624]
Polyphenol			
Terminalia chebula	Chebulagic acid	COX-1, COX-2, 5-LOX	[807]
Curcuma longa	Curcumin	NF-κB, COX-2, STAT-3	[94, 95, 877]
Punica granatum	Punicalagin	NF-κB, COX-2	[181]
Garcinia cambogia	Garcinol, gambogic acid	NF-κB, COX-2, 5-LOX, iNOS	[123, 878, 879]
Zingiber officinale	[6]-Gingerol, shogaol	NF-κB, COX-2	[862, 880]
Sulfur Compound			
Allium sativum	S-Allyl-L-cysteine, allicin, diallyl sulfide, thiacremonone	NF-κB, TNF-α, iNOS, COX-2, IL-6, MCP-1, IL-8, IL-10, MIG, IL-1β	[29, 264, 265, 267, 881]
Triterpine			
Boswellia serrata	Boswellic acid	NF-κB, COX-2, STAT-3, 5-LOX	[61, 882]
Callicarpa macrophylla	Betulinic acid	NF-κB, COX-2, STAT-3	[65, 66]
Trigonella foenum-graecum	Diosgenin	NF-κB, COX-2, STAT-3	[229, 230]
Commiphora mukul	Guggulsterone	NF-κB, STAT-3	[83, 85]
Commiphora wightii	Guggulsterone	NF-κB, STAT-3	[83, 85]
Glycyrrhiza glabra	Glycyrrhizin	iNOS, NF-κB, IL-4, IL-5, IFN-γ	[883, 884]
Ocimum sanctum	Ursolic acid	NF-κB, COX-2, STAT-3	[159, 160]
Withania somnifera	Withanolides	NF-κB, COX-2	[239, 240]
Diterpine			
Andrographis paniculata	Andrographolide, neoandrographolide	NF-κB, TNF-α, IL-6, iNOS, IFN-γ, IL-12p70, COX-2	[278, 279, 283, 291, 293, 294, 885]
Vitex negundo	Negundoin C, E	iNOS, COX-2	[846]
Sesquiterpine			
Saussurea lappa	Cynaropicrin, saussureamines A, B	TNF-α, NF-κB, iNOS	[886–888]

Ayurvedic Plants Alkaloid	Active Compounds	Molecular Targets	References
Terpenoid Lactone			
Azadirachta indica	Azadirachtin	NF-κB, STAT-3	[42]
	Nimbidin, nimbolide	PGE2, IL-1, NF-κB	[43, 183]
Miscellaneous			
Abies pindrow	Pinitol	NF-κB, COX-2	[10]
Aegle marmelos	Marmelin	COX-2, IL-8, TNF-α	[889]
Alpinia galanga	ACA	NF-κB, COX-2, iNOS	[34, 890]
Boerhaavia diffusa	Punarnavine	NF-κB	[53]
Foeniculum vulgare	Anethole	NF-κB, COX-2	[119]
Picrorhiza kurroa	Picroliv	NF-κB, COX-2	[166]
Psoralea corylifolia	Psoralen	IL-10	[178]
Pterocarpus marsupium	Pterostilbene	COX-2	[179]
Solanum nigrum	Phytoglycoprotein	NF-κB, iNOS, COX-2	[891]
Syzygium aromaticum	Eugenol	NF-κB, COX-2	[892]
Tinospora cordifolia	(1,4)-alpha-D-glucan	NF-κB	[893]

5-LOX, 5-lipooxygenase; COX-2, cyclooxygenase-2; IL-1, interleukin (IL)-1; iNOS, inducible nitrogen oxide synthase; IP-10, IFN-γ-induced protein-10; MCP-1, monocyte chemotactic protein-1; MIG, monokine induced by IFN-γ; MIP-α, macrophage inflammatory protein-1 alpha; NF-κB, nuclear factor-kappaB; PAFR, platelet-activating factor-receptor; PGE2, prostaglandin E2; STAT-3, signal transducer and activator of transcription 3; TNF-α, tumor necrosis factor-alpha