



# HHS Public Access

Author manuscript

*Curr Res Compliment Altern Med.* Author manuscript; available in PMC 2022 September 21.

Published in final edited form as:

*Curr Res Compliment Altern Med.* 2022 ; 6(1): . doi:10.29011/2577-2201.100053.

## The Case for Moxibustion for Painful Syndromes: History, principles and rationale

Nigel C Dawes<sup>1</sup> [Senior Collaborator], Joyce K Anastasi<sup>2,\*</sup> [Founding Director]

<sup>1</sup>NYU Special Studies in Symptom Management, NY Kampo Institute, New York, NY, USA

<sup>2</sup>Special Studies in Symptom Management, Independence Foundation Endowed Professor, New York University, New York, NY, USA

### Abstract

Traditional Chinese Medicine (TCM) has evolved over thousands of years. TCM practitioners use various approaches (such as acupuncture and tai chi) as well as herbal products to address health problems. Though lesser known in the west, the practice of Moxibustion is an integral part of Traditional East Asian Medicine. Moxibustion is an important non-invasive treatment that has shown to be beneficial in treating painful syndromes including neuropathy. It has been suggested that moxibustion may alleviate neuroinflammation by inhibiting NF-kB and by activating Nrf2. These anti-inflammatory and protective mechanisms could be key to exploring the use of moxibustion in treating other etiologies of neuropathy including HIV. There is ample scope for future study in this area and consideration of the history, development and practical applications of moxibustion therapy may be of help in this regard. This article seeks to explore the background, principles, and application of moxibustion in the clinical setting with particular emphasis on its potential for symptom management in the treatment of neuropathy and pain.

### Introduction

Traditional Chinese Medicine (TCM) has evolved over thousands of years. TCM practitioners use various approaches (such as acupuncture and tai chi) as well as herbal products to address health problems [1]. Though lesser known in the west, the practice of Moxibustion is an integral part of Traditional East Asian Medicine. The fact is, Acupuncture and Moxibustion come as a pair and in Chinese and Japanese, they are two characters that make up one word (針灸 Zhenjiu or Shinkyu) forming one mode of therapy [2]. “Acumoxa” is a hybrid word of “acupuncture” and “moxibustion” that more closely resembles the Chinese ideograph for this treatment [3].

Moxibustion, is a non-invasive therapy that involves burning moxa, the dried herb *Artemisia vulgaris*, on or above the skin at acupoints, warming them, in order to alleviate symptoms [4]. The term moxibustion derives from the name of the wormwood plant most frequently used, *Artemesia Moxa* or (Japanese) *A. Mogusa* [5].

\*Corresponding author: Joyce K Anastasi, Founding Director, Special Studies in Symptom Management, Independence Foundation Endowed Professor, New York University, New York, NY, USA.

Moxibustion has been practiced along with acupuncture in China for thousands of years for the prevention and treatment of disease. Its clinical efficacy relies on the transmission of thermal effect to specific points and areas on the body surface effecting vascular and other changes. The practice has undergone extensive refinement in Japan where, since the Edo Period (1603–1867) in particular, moxibustion has been used widely in the management of pain and for health maintenance and disease prevention.

Its therapeutic mechanism has been studied [6,7] and it is widely used to treat various disorders [8] including correcting breech presentation [9], treating dysmenorrhea [10], constipation [11], prostatitis [12], chronic fatigue syndrome [13], osteoarthritis [14–20] and pain, [21,22] including low-back pain [23,24] and peripheral neuropathy [25].

With regard to the treatment of peripheral neuropathy, in particular, it has been shown that moxibustion: “inhibited the protein and mRNA expression of NF-κB but induced the protein and mRNA expression of Nrf2 in the sciatic nerve. Moxibustion restored the balance between NF-κB and Nrf2. Thus, neural inflammation was relieved by regulating interleukin factors” [26]. It is this anti-inflammatory effect that accounts for its use in treating all manner of pain and inflammation such as those specific conditions mentioned above, including peripheral neuropathy.

The theory of Chinese Medicine dictates that the stimulation of specific points on the body by moxibustion can produce the effect of regulating Qi and Blood flow, dredging the meridians, and regulating functions [27]. This treatment can also promote the elimination of contaminants and alleviate the pathological effects, such as inflammation, adhesion, exudation, and hematoma [28]. According to traditional theory, pain is a manifestation of blockage in the normal flow of Qi and blood through the meridians, and both acupuncture, moxibustion and massage, and other manipulative therapies used in East Asian Medicine all aim at restoring the normal flow within this network. In this paradigm, pain and sensory disruption are directly related to impairment in the normal flow of Qi and Blood according to traditional thinking.

To appreciate the potential of moxibustion in the treatment of pain and inflammation and in particular peripheral neuropathy, it will be important to consider both the history and background of this ancient therapy as well as the methodology of its application and perceived mechanisms.

## History and Origins

In contrast to the development of Western medicine, which can be traced back to Hippocrates via a clear and distinct route, Chinese acumoxa theory was already fully developed by the end of the 2<sup>nd</sup> century BCE. In 1972, documents written on bamboo and silk scrolls were discovered in the Mawangdui tombs (sealed in 168 BCE) in Changsha, Hunan Province, China. The discovery included documents such as the *Yinyang Shiyi Maijiujing* (‘Moxibustion Canon of the Eleven Yin and Yang Vessels’) and the *Zubi Shiyi Maijiujing* (‘Moxibustion Canon of the Eleven Vessels of the Foot and Forearm’) which only relate to moxibustion and do not include any references to acupuncture or acupoints. The

documents' referencing of eleven lines of channels (meridians), suggests that the origins of moxibustion and of meridians are earlier than those of acupuncture and acupoints [29].

In the Huangdi Neijing ("The Yellow Emperor's Inner Cannon" dating from the second century BCE), a fundamental doctrinal source of Chinese Medicine for over 2 millennia, there is reference to the likely rationale for the origins of moxa use: "The north is the region where heaven and earth close up and store. The land is high and the people dwell in mounds. There is wind, cold, and crystal-clear ice. The people enjoy the wilderness and drink milk. Their viscera are cold, which engenders the disease of fullness. The appropriate treatment is to burn moxibustion [30]." In other words, in colder climates, it was natural for primitive societies to seek warmth and protect themselves with fire.

Indeed, the origins of moxibustion are inextricably linked to the significance of fire in ancient Chinese culture. Fire belongs to Yang in Yin/Yang theory and is associated with the active, warming, energizing dynamic in nature. The fire element, along with those of water, metal, earth, and wood constitute one of the core theoretical frameworks of Traditional Chinese Medicine known as "Five-phase theory" which, along with Yin/Yang theory, still underpins traditional medical practice to this day throughout East Asia. Mastering the fire-making technique provided a prerequisite for moxibustion to take its shape. In cooking a meal or getting warm by using fire [31], people unexpectedly found that stimulating specific locations on the body could alleviate pain and suffering.

In pre-Han dynasty China, fire was used by Shamans in the exorcistic practices of steaming and cauterization using Moxa (mugwort) whose heat and vapors were thought to be effective in expelling disease-causing "demons". Since solar fire was considered the ultimate life-giving heat source, the practice of moxibustion originally involved the lighting of moxa using a type of mirror or "solar speculum" manipulated by the Shaman to conduct the celestial (Yang) energy of the sun into the earthly (Yin) energy of the plant thus combusting it. This process, it was believed, could penetrate the vessels of an afflicted person and expel noxious spirits as well as strengthen their defensive energies [32].

As Chinese Medicine evolved and became more systematized, fire assumed specific significance in both physiology and pathology, departing from the shamanistic beliefs that disease was caused by demonic influences. In physiological terms, fire was seen as a metaphor for all the Yang functions of the body, in particular the Spleen Yang or "digestive fire" (referring to the function of the gastrointestinal tract) and the Kidney Yang or "Mingmen fire" (a more esoteric concept referring inclusively to the functions of the urogenital and reproductive systems as well as adrenal and endocrine functions as a whole). In this context, prophylactic moxibustion was seen as a way to improve functionality of these systems thereby promoting better health.

In pathological terms fire became associated in Chinese Medicine with "evil" or pathogenic heat that had either invaded from the outside (micro-organisms) or had been engendered within the body (inflammation) which then required "purging" or "cooling" therapies respectively. Moxibustion was used traditionally both to drive pathogens from the body as well as to warm the Qi and stimulate circulation of blood and reduce inflammation. Indeed,

current TCM theory holds that moxibustion has a dual effect of tonification and purgation [33].

During the Ming dynasty (1368–1644) in China, partly due to moveable type and block printing, the number of publications dedicated to moxibustion increased exponentially, amongst them most notably the works of Li Shizhen [34], Yang Jizhou [35] and Zhang Jiebin [36] which detailed the specifics of moxibustion treatment including the different materials used, the methods and techniques, patient positioning, indications, and contraindications [37].

In Japan, where Chinese Medicine transmission began from the 6thCE onward, not only the ancient pharmacopeia, but literary works of all periods make reference to moxibustion from Murasaki Shikibu's eleventh-century Tale of *Genji* onward [38], reaching its peak in the Edo period when many of the unique aspects of Japanese moxibustion techniques began to emerge. Nowadays, outside of the medical setting, moxibustion is a common home remedy in Japan where it is used almost exclusively by older women and men or for children [39]. A prominent medical anthropologist has noted that: “traditionally moxa was used as a form of chastisement for young children” concluding that: “the use of moxa is associated in the minds of many older Japanese with their childhood and the inducement of behavioral changes that restore good family relationships [40].” As in China, moxibustion also had historic links with religious practices and to this day many Buddhist temples in Japan are known for their moxibustion treatments [41].

Since the Edo period, moxibustion (along with acupuncture and Shiatsu massage) has traditionally been the occupation of the blind in Japan [42] though nowadays professional training leading to a license to practice is required and moxibustion is most commonly practiced by acupuncturists and Shiatsu therapists.

One of the unique features of moxibustion today in Japan is that direct moxa therapy (see materials and methods section below) is commonplace, whereas indirect moxibustion with the use of moxa sticks is used more frequently in China [43]. The earliest record of the use of a moxa stick appeared in the “Medical Secrets of an Official” (Waitai Miyao) from the Tang dynasty [44], making this technique a relative newcomer in the history of moxibustion therapy.

### **Moxibustion and Methods**

Acupuncture and Moxibustion are similar regarding their respective stimulation of acupuncture points along the meridians [45]. However, unlike acupuncture which uses mechanical stimulation, moxibustion is primarily a type of thermal stimulation with burning dried plant materials (*Artemisia moxa*) [46].

An explanation for the use of moxa wool (shredded artemisia) is that it grows everywhere, so is cheap and easy to get, it readily holds its shape in cones, and its burning characteristics are ideal: it burns slowly, stays lit, produces an even heating, and has a pleasant fragrance [47].

It can be applied either with a small amount of burning moxa directly on the skin (direct moxibustion) or with heat generated from burning moxa 3–5 cm away from the skin surface (suspended or indirect moxibustion, supplementary) [48].

The effects in each case of indirect or direct moxibustion are quite different with the thermal and infra-red effects of the former (described in the next section) being key whilst direct moxibustion provides stimulation by denatured proteins (whereby histotoxins are released in the serum and stimulate the production of red and white blood cells) [49].

There are distinctly different grades of moxa material used with the lower grades including the dried leaves, veins and twigs mixed together which burn at a higher temperature and are suitable for indirect moxibustion, in particular stick moxa. Pure and ultra-pure moxa is produced by extracting all the impurities from the dried leaves leaving only the “wool” which is light and aerated, burning more quickly, more uniformly, and at a lower temperature making it suitable for direct moxibustion.

Direct moxibustion, commonly practiced in Japan, is called Okyu (Thread Moxa) and involves the rolling of small pieces of ultra-pure moxa wool into thin, string-like threads. These threads can vary in diameter so that when small pieces of them are pinched off they will form strands that are then placed vertically on the skin to be cauterized. Typically, there are about 4 sizes of these threads used in Japan: string-like, sesame size, half rice grain size, and rice grain size. The size of the thread determines the level of heat stimulation delivered and this can be controlled by using a bamboo tube, glass, or cup, placed over the burning moxa to control the oxygen flow and thus regulate the rate and temperature of cauterization [50]. Less commonly, there is a form of direct moxibustion called Dano Kyu (suppurative moxibustion) where larger moxa cones are cauterized on specific points (usually on the back) and a special ointment is then applied to the burn to encourage the discharge of pus [51].

Indirect moxibustion techniques are many. In Japan, the main two techniques used are Chinnetsu Kyu (sensing heat moxa) which originates from Osaka. In this technique, a cone of moxa the size of an aduki bean is burned on the skin. The moment the patient senses the heat he/she will give a signal and the cone is immediately removed without burning them. The procedure is repeated until the patient reports a penetrating feeling of heat in the area on and around the point. The second technique of indirect moxibustion is called Kyu To Shin (needle moxa) whereby a small ball of moxa is attached to the handle of an acupuncture needle already inserted at a specific point and ignited. The warmth generated by the moxa thus passes down the needle and penetrates the point again without burning the patient. This technique is also current in China [52].

Other indirect moxibustion techniques involve using various materials to insulate the skin from the burning moxa by placing the moxa wool on top of the material which then rests on the skin surface before igniting. Common materials used include: ginger (to increase the warming effect and improve circulation), garlic (to relieve swelling and pain); salt (at the umbilicus to rescue Yang) and aconite (to warm Kidney Yang) [53]. There are also moxa boxes which are filled with ignited moxa wool raised off the body surface by a metal gauze

inside the box. They warm a larger area of the body rather than a single point or points (such as the low back or abdomen).

Finally, there is the moxa stick, commonly used in China, which resembles the shape of a cigar and is lit at one end to provide the indirect heat source. So-called mild-warm moxa involves holding the lighted stick 2–3 cm from the skin warming the area until it becomes red (without burning). Another stick technique is called sparrow-pecking moxibustion where the lighted stick is moved up and down, left and right or round and round at a point allowing for more control of the heat delivery [54].

## Mechanisms

Since the methods of acupuncture and moxibustion are different, there are functional distinctions between them. Acupuncture generally makes the body release heat (anti-inflammatory) and seeks to eliminate pathogens while moxibustion mainly warms the body and recruits healthy *Qi* [55]. Indeed, pre-clinical studies have suggested that moxibustion can boost the immune system [56,57]. In short, moxibustion exerts antinociceptive [58], anti-inflammatory [59], and immunomodulatory [60] effects in humans [61].

Amongst these effects, the heat stimulation and chemical action of ignited moxa is the most important variable for moxibustion [62]. A “heat sensation” phenomenon in a large proportion of patients receiving suspended (indirect) moxibustion treatment has been observed [63]. It has been shown that the thermal effect of moxibustion has a close relation to the Warm Receptors (WRs) and/or the polymodal receptors (PRs) and the antipyretic and thermolytic effects of moxibustion are achieved by stimulating polymodal receptors of acupoints [64–66]. The impact of the local heat stimulus was studied in the laboratory to follow-up on the suggestion that the production of inflammation mediators, mainly histamine, at the site of moxa applied skin were important to the impact of moxibustion therapy [67]. A number of clinical trials have shown that the appearance of heat sensitization is correlated with better therapeutic effects in various diseases, indicating the clinical significance of such responses [68–73]. These studies suggest a potential link between the sensitization responses induced by moxibustion and its modulatory effects on pain and inflammation. The question remains as to whether such effects are directly due to the heat stimulation, the mugwort effect, or the combination of the two [74].

It seems clear however that a primary feature of moxibustion remains the unique nature of the heat stimulus itself which, rather than dispersing over the skin surface in a diffuse manner (such as the infrared heat from a heat lamp), penetrates deeply into underlying tissues at the precise location of acupoints. It is likely that this is the reason why, in Japan, it is known as “penetrating moxibustion”. The concentration of this heat stimulus may be compared to a laser and thus is highly effective at reducing pain and inflammation [75]. The Yellow Emperor’s Classic of Internal Medicine also had the theory of “removing the stagnation of fire by heat” (*Yi Re Yin Re*). Moreover, the results of much clinical research supported the idea that “heat syndrome could be treated by moxibustion” [76,77].

Specifically, in regard to its heat stimulus and analgesic effects, it has been suggested that moxibustion may alleviate neuroinflammation by simultaneously inhibiting Nuclear Factor

Kappa B (NF- $\kappa$ B), which controls cytokine production, and by activating nuclear factor erythroid 2-related factor 2 (*NRF2*) which helps regulate inflammation[78].

Additionally, it has been shown that temperature should be taken into account for moxibustion treatment in chronic inflammatory and neuropathic pain, with a stronger analgesic effect achieved at higher temperatures between 47–52°C as opposed to between 37–42°C [79]. Finally, in terms of potential therapeutic mechanisms of moxibustion, its pharmacological actions must also be considered. The oils contained in the *Artemisia* plant have a variety of biological activities such as the expansion of airway smooth muscle, relieving cough, expectorant effect, and strong antioxidant activity [80–82]. The moxa is rich in flavonoids and polysaccharides, which have strong antioxidant activity too [83,84]. The effect of these active ingredients is increased rather than being destroyed after burning and can be enhanced by the use of auxiliary materials such as garlic and ginger on which the burning moxa is placed for specific therapeutic aims [85–87].

There have been many viewpoints on the mechanism of moxibustion effects, such as the thermal stimulation effect, non-specific autologous protein therapeutics, non-specific stress responses, and aromatherapy. The generally accepted view is that the meridian system combines with the physical and chemical effects of moxibustion to produce comprehensive effects. In spite of all the research to date, much still remains to be understood regarding the detailed mechanisms of moxibustion.

## Conclusion

This article has attempted to underline the clinical significance of moxibustion within the practice of traditional East Asian Medicine and by extension to suggest a potential role for it within contemporary integrated medical practice, especially in the area of managing pain and neuropathy. By offering evidence of its long history, principles, and therapeutic rationale and some of the perceived mechanisms of its effect both from a traditional and scientific perspective, it is hoped that the treatment potential of this much-undervalued therapy can be more easily recognized, understood, and utilized. There remains a strong case for further investigation into the clinical potential of moxibustion for the management of neuropathic pain syndromes.

## Funding

Research reported in this manuscript was supported in part by the National Institute of Nursing Research of the National Institutes of Health under Award Number R01-NR017917. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

## References

1. National Institutes of Health/NCCIH. (2022). *Traditional Chinese Medicine: What You Need To Know*. Bethesda, MD.
2. Brown S., Foreword, *North American Journal of Oriental Medicine*, Vol.1, No.1, July 1994.
3. Chiu J-H (2013) How Does Moxibustion Possibly Work? *Evid Based Complement Alternat Med*.
4. Lao L. *Traditional Chinese Medicine, Part III, Chapter 12. Essentials of Complementary and Alternative Medicine*. Ed. Jonas WB, Levin JS 1999, Philadelphia: Lippincott Williams & Wilkins, p219–232.

5. Encyclopedia Britannica, Health and Medicine, Moxibustion.
6. Chiu J-H (2013) How Does Moxibustion Possibly Work?. *Evid Based Complement Alternat Med*.
7. Lee MS, Kang JW, Ernst E (2010) Does moxibustion work? An overview of systematic reviews. *BMC Res Notes* 3: 284. [PubMed: 21054851]
8. Wang LL, Wang XJ, Zhang JB (2012) To recognize the emergency and understand the value of moxibustion: book review of bei ji Jiu fa (Moxibustion for Emergency). *Zhongguo Ahen Jiu* 32: 941–945.
9. Cardini F, Weixin H (1998) Moxibustion for correction of breech presentation: a randomized controlled trial. *JAMA* 280: 1580–1584. [PubMed: 9820259]
10. Yang M, Chen X, Bo L, Lao L, Chen J, et al. (2017) Moxibustion for pain relief in patients with primary dysmenorrhea: A randomized controlled trial. *PLoS One* 12: e0170952. [PubMed: 28170396]
11. Park JE, Sul JU, Kang K, Shin BC, Hong KE et al. (2011) The effectiveness of moxibustion for the treatment of functional constipation: a randomized, sham-controlled, patient blinded, pilot clinical trial. *BMC Complement Altern Med* 11: 124. [PubMed: 22132755]
12. Cao Q, Zhou X, Chen J, Zhong Y, Zhang H, et al. (2019) Efficacy and safety of moxibustion in patients with chronic prostatitis/chronic pelvic pain syndrome: A systematic review protocol. *Medicine (Baltimore)* 98: e15678. [PubMed: 31096505]
13. Xue K, Wang Y, Wang X, Chen P, Xiao C, et al. (2021) The efficacy and safety of moxibustion for chronic fatigue syndrome: A protocol for systematic review and meta-analysis. *Medicine (Baltimore)* 100: e25742. [PubMed: 33950958]
14. Xu X, Wang MM, Sun ZL, Zhou DP, Wang L, et al. Discovery of serum proteomic biomarkers for prediction of response to moxibustion treatment in rats with collagen-induced arthritis: an exploratory analysis. *Acupunct Med* 34: 184–193. [PubMed: 26541191]
15. Zhao L, Cheng K, Wang L, Wu F, Deng H, et al. (2014) Effectiveness of moxibustion treatment as adjunctive therapy in osteoarthritis of the knee: a randomized, double-blinded, placebo-controlled clinical trial. *Arthritis Res Ther* 16: R133. [PubMed: 24962039]
16. Li ZD, Cao LH, Wang SC (2009) Effect of moxibustion in treating knee joint osteoarthritis and its relation with contents of hyaluronic acid in serum and synovial fluid. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 29: 883–885. [PubMed: 20073216]
17. Li JW, Xiang SY, Ma ZY, Feng YB, Tong HY, et al. (2008) Clinical observation on cake-separated mild-warm moxibustion for treatment of knee osteoarthritis. *Zhongguo Zhen Jiu* 28: 17–19. [PubMed: 18257181]
18. Sun K, Yang J, Shen DK (2008) Clinical observation on treatment of primary knee osteoarthritis of liver and kidney deficiency type with Aconite cake-separated moxibustion. *Zhongguo Zhen Jiu* 28: 87–90. [PubMed: 18405148]
19. Fu Y, Kang MF, Chen RX, Zhang B, Zhang HF (2007) Observation on the therapeutic effect of painless festering moxibustion on knee osteoarthritis. *Zhongguo Zhen Jiu* 27: 513–515. [PubMed: 17722832]
20. Su JC, Cao LH, Li ZD, Wang SC, Zhang QJ, et al. (2009) Controlled clinical trials of initial observation on therapeutic effects of moxibustion for osteoarthritis of the knee: multi-center clinical effect. *Zhongguo Gu Shang* 22: 914–916. [PubMed: 20112574]
21. Zhou W, Lei R, Zuo C, Yue Y, Luo Q, et al. (2017) Analgesic Effect of Moxibustion with Different Temperature on Inflammatory and Neuropathic Pain Mice: A Comparative Study. *Evid Based Complement Alternat Med*.
22. Lee MS, Choi TY, Kang JW, Lee BJ, Ernst E (2010) Moxibustion for treating pain: a systematic review. *Am J Chin Med* 38: 829–838. [PubMed: 20821815]
23. Leem J, Lee S, Park Y, Seo BK, Cho Y, et al. (2017) Effectiveness and safety of moxibustion treatment for non-specific lower back pain: protocol for a systematic review. *BMJ Open* 7:e014936.
24. Dubois MY, Chen L (2014) Of Low Back Pain and Moxibustion. *Pain Medicine* 15: 1243–1244. [PubMed: 25132305]



25. Li J, Hu X, Liang F, Liu J, Zhou H, et al. (2019) Therapeutic effects of moxibustion simultaneously targeting Nrf2 and NF- $\kappa$ B in diabetic peripheral neuropathy. *Appl Biochem Biotechnol* 189: 1167–1182. [PubMed: 31209719]
26. Ibid.
27. Hinman RS, McCrory P, Pirotta M, Relf I, Crossley KM, et al. (2012) Efficacy of acupuncture for chronic knee pain: protocol for a randomised controlled trial using a Zelen design. *BMC Complement Altern Med* 12:161. [PubMed: 22992309]
28. Yuan YD, Zhao XP, Deng ZL, Song QH, Zhang LY, et al. (2015) Interference of strength training can obviously increase the effect of moxibustion treatment on patients with knee joints injuries. *Int J Clin Exp Med* 8: 13748–13754. [PubMed: 26550321]
29. Chen Y (1997) Silk scrolls: earliest literature of meridian doctrine in ancient China. *Acupunct Electrother Res* 22: 175–189. [PubMed: 9494626]
30. Veith I, *The Yellow Emperor's Classic of Internal Medicine*, University of California Press, Berkley, 1972.
31. Run-Ming Y (1985) The origin and development of Chinese acupuncture and moxibustion. *Anc Sci Life* 4: 224–228. [PubMed: 22557484]
32. Jianmin L (2002) Fire and the Origins of Moxibustion. *Studies In The History of Natural Sciences*.
33. Deng H, Shen X (2013) The mechanism of moxibustion: ancient theory and modern research. *Evid Based Complement Alternat Med* 2013:379291. [PubMed: 24159344]
34. *Bencao Gangmu (Compendium of Materia Medica)*, Nanjing, 1596.
35. *Zhen Jiu Da Cheng (Great Compendium of Acupuncture and Moxibustion)*, 1601
36. *Lei Jing (Illustrated Supplement to the Categorized Classic)*, 1624.
37. Wilcox L (2008) *Moxibustion: The Power of Mugwort Fire*. Blue Poppy Press.
38. Lock M (1980) *East Asian Medicine in Urban Japan*. University of California Press pp:94.
39. Ibid. pp.94
40. Ibid. pp.96
41. Ohnuki-Tierney E., *Illness and Culture in Contemporary Japan*, Cambridge University Press, 1984, pp.113.
42. Ibid. pp.113
43. Mizutani J., *Practical Moxibustion Therapy (2)*, North American Journal of Oriental Medicine, Vol.2, No.2, November 1994, pp.22.
44. Huang LX (1995) A study of the origin and development of moxibustion. *Journal of Clinical Acupuncture and Moxibustion* 9: 11–12.
45. World Health Organization Western Pacific Region, *WHO Standard Terminologies on Traditional Medicine in the Western Pacific Region*, WHO Regional Office for the Western Pacific, Manila, Phillipines, 2007.
46. Joos S, Brinkhaus B, Maluche C, Maupai N, Kohnen R, et al. (2004) Acupuncture and Moxibustion in the treatment of active Crohn's disease: a randomized controlled study. *Digestion* 69: 131–139. [PubMed: 15114043]
47. O'Connor J, Bensky D (translators), *Acupuncture: A Comprehensive Text*, Eastland Press, Seattle, WA, 1981.
48. Liao F, Zhang C, Bian Z, Xie D, Kang M, et al. (2014) Characterizing Heat-Sensitization Responses in Suspended Moxibustion with High-Density EEG. *Pain Med* 15: 1272–1281. [PubMed: 25132308]
49. Mizutani J. *Practical Moxibustion Therapy (4)*, North American Journal of Oriental Medicine, Vol.2, No.4, July 1995, pp.18.
50. Mizutani J. *Practical Moxibustion Therapy (1)*, North American Journal of Oriental Medicine, Vol.1, No.4, July 1994, pp.15.
51. Ibid, pp.17
52. Mizutani J. *Practical Moxibustion Therapy (5)*, North American Journal of Oriental Medicine, Vol.2, No.5, November 1995, pp.31.

53. Dharmananda S (2004) Moxibustion: Practical Considerations for modern use of an ancient technique. ITM
54. Ibid
55. Kang SB, Medical Classics of Acupuncture and Moxibustion, Iljoongsa, Seoul, Republic of Korea, 2000.
56. Yamashita H, Ichiman Y, Tanno Y (2001) Changes in peripheral lymphocyte subpopulations after direct moxibustion, *Am J Chin Med* 29: 227–235. [PubMed: 11527066]
57. Kung YY, Chen FP, Hwang SJ (2006) The different immunomodulation of indirect moxibustion on normal subjects and patients with systemic lupus erythematosus. *Am J Chin Med* 34: 47–56. [PubMed: 16437738]
58. Kim JH, Kim HK, Park YI, Sohn IC, Choi DO, et al. (2006) Moxibustion at ST36 alleviates pain in complete Freund's adjuvant-induced arthritic rats. *Am J Chin Med* 34:57–67. [PubMed: 16437739]
59. Lu J, Zhang HL, Yin ZZ, Tu Y, Li ZG, et al. (2012) Moxibustion attenuates inflammatory response to chronic exhaustive exercise in rats. *Int J Sports Med* 33: 580–585. [PubMed: 22510802]
60. Han JB, Oh SD, Lee KS, Choi KS, Cho YW, et al. (2003) The role of the sympathetic nervous system in moxibustion-induced immunomodulation in rats. *J Neuroimmunol* 140: 159–162. [PubMed: 12864984]
61. Liao F, Zhang C, Bian Z, Xie D, Kang M, et al. (2014) Characterizing Heat-Sensitization Responses in Suspended Moxibustion with High-Density EEG. *Pain Med* 15: 1272–1281. [PubMed: 25132308]
62. Im ST, Kim KH, Kim KS (1994) A study of physical characteristics of moxibustion. *The Journal of Korean Acupuncture and Moxibustion Society* 11: 327–336.
63. Xie D, Liu Z, Hou X, Zhang B, Xiong J, et al. (2013) Heat sensitization in suspended moxibustion: features and clinical relevance. *Acupunct Med* 31: 422–424. [PubMed: 24008013]
64. Dong QS, Xian MQ, Dong XM, et al. (1998) Relation of moxibustion therapy to cutaneous receptors. *World Journal of Acupuncture—Moxibustion* 8: 32–39.
65. Dong QS, Xian MQ, Dong XM, et al. (2000) Antipyretic action of moxibustion and its relation to acupoint receptors. *World Journal of Acupuncture—Moxibustion* 10: 31–35.
66. Xian MQ, Dong QS, Zhang SH, et al. (2000) Thermolytic effect of moxibustion and its relation to acupoint receptors. *World Journal of Acupuncture—Moxibustion* 10:24–31.
67. Okazaki M, Aizawa S, Yamauchi M, Oguchi K (1990) Effects of a single moxibustion on cutaneous blood vessel and microvascular permeability in mice, *Am J Chin Med* 18: 121–130. [PubMed: 2270846]
68. Chen R, Chen M, Xiong J, Su T, Zhou M, et al. (2013) Influence of the deqi sensation by suspended moxibustion stimulation in lumbar disc herniation: study for a multicenter prospective two arms cohort study. *Evid Based Complement Alternat Med*.
69. Chen R, Xiong J, Chi Z, Zhang B (2012) Heat-sensitive moxibustion for lumbar disc herniation: a meta-analysis of randomized controlled trials. *J Tradit Chin Med* 32(3):322–328. [PubMed: 23297550]
70. Chen M, Chen R, Xiong J, Chi Z, Sun J, et al. (2012) Evaluation of different moxibustion doses for lumbar disc herniation: multicentre randomised controlled trial of heat-sensitive moxibustion therapy. *Acupunct Med* 30:266–272. [PubMed: 22858560]
71. Chen R, Chen M, Xiong J, Su T, Zhou M, et al. (2013) Comparative effectiveness of the deqi sensation and non-deqi by moxibustion stimulation: a multicenter prospective cohort study in the treatment of knee osteoarthritis. *Evid Based Complement Alternat Med*.
72. Chen R, Chen M, Xiong J, Chi Z, Zhou M, et al. (2012) Is There Difference between the Effects of Two-Dose Stimulation for Knee Osteoarthritis in the Treatment of Heat-Sensitive Moxibustion?. *Evid Based Complement Alternat Med*.
73. Chen R, Chen M, Xiong J, Chi Z, Zhang B, et al. (2013) Curative effect of heat-sensitive moxibustion on chronic persistent asthma: a multicenter randomized controlled trial. *J. Tradit Chin Med* 33:584–591. [PubMed: 24660579]
74. Dubois MY, Chen L (2014) Of Low Back Pain and Moxibustion. *Pain Med* 15: 1243–1244. [PubMed: 25132305]

75. Mizutani J (1994) Practical Moxibustion Therapy (1), North American Journal of Oriental Medicine 1:14.
76. Li XW, Yang YK, Xie XM, Bai LN, Zhang XS (2012) Economic evaluation of treating herpes zoster with various methods of acupuncture and moxibustion. J Tradit Chin Med 32: 125–128. [PubMed: 22594116]
77. Park JE, Lee MS, Jung S, Kim A, Kang K, et al. (2009) Moxibustion for treating menopausal hot flashes: a randomized clinical trial. Menopause 16: 660–665. [PubMed: 19293729]
78. Li J, Hu X, Liang F, Liu J, Zhou H, et al. (2019) Therapeutic effects of moxibustion simultaneously targeting Nrf2 and NF- $\kappa$ B in diabetic peripheral neuropathy. Appl Biochem Biotechnol 189: 1167–1182. [PubMed: 31209719]
79. Zhou W, Lei R, Zuo C, Yue Y, Luo Q, et al. (2017) Analgesic Effect of Moxibustion with Different Temperature on Inflammatory and Neuropathic Pain Mice: A Comparative Study. Evid Based Complement Alternat Med.
80. Xie Q, Bian R, Yang Q, et al. (1999) Studies on the respiratory pharmacology of essential oil extracted from *Artemisia argyi*-I, Bronchodilating, antitussive and expectorant effects. Chinese Journal of Modern Applied Pharmacy 16: 16–19.
81. Huang HC, Wang HF, Yih KH, Chang LZ, Chang TM (2012) Dual bioactivities of essential oil extracted from the leaves of *Artemisia argyi* as an antimelanogenic versus antioxidant agent and chemical composition analysis by GC/MS. Int J Mol Sci 13:14679–14697. [PubMed: 23203088]
82. Hitosugi N, Ohno R, Hatsukari J, Mizukami S, Nagasaka H, et al. (2001) Diverse biological activities of Moxa extract and smoke. In Vivo 15:249–254. [PubMed: 11491021]
83. Guo C (2001) A comparative study of the volatile oil from Shandong and wild folic Artemisia. Chinese Traditional and Herbal Drugs 32: 500–503.
84. Wang L, Lu J, Gu C (2001) Microwave method for the determination of the total content of volatile oil in the different seasons mugwort leaf. Journal of Mathematical Medicine 4: 287.
85. Zhao J, Jia C, Tian Y (1999) Latest 10 years progress of moxibustion experimental study in Japan. Chinese Acupuncture & Moxibustion 8: 507–511.
86. Motoyo O, Shizuo T, Kazuo T, et al. (1991) A study on radical scavenging with moxibustion product. Journal of the Japan Society of Acupuncture 41: 42.
87. Ikuko N, Nobuo U (1988) The antioxidative substance in the products of burned moxa. Journal of the Japan Society of Acupuncture 38: 39.