Additional material

Table A Traditional utilization of amla and the relevant pharmacological properties

Traditional utilization	**Relevant pharmacological properties**
Anti-cancer activity	- Methanol extract of amla decreased the level of thiobarbituric acid reactive substance (TBARS) and enhanced the activities of enzymatic and non-enzymatic antioxidants in the tumor-bearing animals[1]. - Amla fruit juice significantly suppressed TBARS, lipid profile, and estrogen/progesterone receptor levels as well as reversed the status of antioxidant to near normal level in the cancer-bearing animals[2]. - Silver nanoparticles synthesized using the aqueous extract of amla enhanced cytotoxicity in laryngeal cancer cells (Hep2 cell line) through oxidative stress and apoptotic function[3]. - Aqueous solution of amla significantly increased the expression of autophagic proteins beclin 1 and LC3B-II as well as significantly inhibited the expression of several angiogenic genes *in vitro* and *in vivo* models[4]. - Amla extract suppressed the proliferation and induced apoptosis independent of p53, a tumor suppressor gene, in human colon cancer stem cells. The suppression of cell proliferation was mediated by targeting the Wnt/b-catenin signaling pathway and inhibiting the expression of c-Myc and cyclin D1[5].
Anti-diabetic effect	- Aqueous extract of amla significantly stimulated the insulin secretion, enhanced the insulin action, and inhibited protein glycation and starch digestion in cell culture model[6].
Anti-inflammatory activity	- Free and bound phenolic compounds of ethanol extract of amla showed the reduction in acute and chronic inflammation in the rat model[7]. - Amla extract potentially and significantly reduced lipopolysaccharide (LPS)-induced tissue factor expression and von Willebrand factor release in human umbilical vein endothelial cells. The extract also significantly decreased LPS-induced adhesion of human monocytic cells to human umbilical vein endothelial cells, as well as reduced the expression of endothelial-leucocyte adhesion molecule-1 in the target cells. Additionally, the extract significantly decreased the concentrations of pro-inflammatory cytokines, TNF-a and IL-6, in serum in rat model[8]. - Methanol extract of amla showed the high antioxidant activities and the decrease in inflammation in rat model by significant reduction of the inflammatory cytokines, IL-1 and TNF-a[9].
Anti-microbial activity	- Aqueous infusion and decoction of amla showed the potent anti-microbial activity against *Staphylococcus aureus*, *S. hemolyticus*, *S. saprophyticus*, *Micrococccus varians*, *M. lylae*, *M. roseus*, *M. halobius*, *M. sedenterius*, *Bacillus subtilis*, *B. megaterium*, and *Candida albicans*[10].

Traditional utilization	Relevant pharmacological properties
	- Ethanol extract of amla exhibited the inhibitory effect on growth of methicillin resistant *Staphylococcus aureus*, *Vibrio cholerae*, and *Pseudomonas aeruginosa*[11].
Treatment of various gastric ailments: peptic ulcer, indigestion, and constipation	- Ethanol extract of amla significantly inhibited the development of gastric lesions as well as significantly decreased the pyloric-ligation induced basal gastric secretion, titratable acidity, and gastric mucosal injury. Additionally, the extract demonstrated the protection against ethanol-induced depletion of stomach wall mucus and the reduction in non-protein sulfhydryl concentration[12]. - Methanol extract of amla showed the ulcer protective effects in the different acute gastric ulcer models in rat model and significantly healed the ulcer lesion. Also, the extract significantly decreased the offensive factors like acid and pepsin as well as increased the defensive factors like mucin secretion, cellular mucus, and life span of mucosal cells[13]. - Methanol extract of amla and its fractions showed the prokinetic and laxative activities in mice model along with the spasmodic effect in the isolated tissues of guinea pig and rabbits. Its activity might partially be mediated through activation of muscarinic receptors[14].
Adaptogenic activity	- Amla extract strengthened the defense mechanisms against free radical damage induced during stress. Its activity appeared to mediate through prostaglandin release and antioxidative action[15].
Rejuvenating activity	- Ethyl acetate extract of amla fruit exhibited the significant decrease in the lipid levels in serum and liver by increasing hepatic peroxisome proliferator-activated receptor (PPAR)-α protein levels, the key regulator of lipid and cholesterol metabolism, as well as reduced the inducible nitric oxide synthase and cyclooxygenase-2 expression levels by inhibiting NF-kB activation in the young and aged rat model[16]. - Hydroalcoholic solution of amla stimulated the fibroblast proliferation and induced the production of procollagen. The extract also decreased the matrix metalloproteinase (MMP)-1 production and significantly increased tissue inhibitor of metalloproteinase (TIMP)-1 [17].
Promoting health and longevity	- Amla extract significantly increased the longevity, fertility, ovarioles number along with the development time in fruit fly (*Drosophila melanogaster*) model[18]. - Amla juice significantly increased the life span of *Drosophila* flies by its high antioxidant property[19].

Table B Compositions of base and PE gels

Ingredient	Base gel (%, w/w)	PE gel (%, w/w)
Propylene glycol Glycerin DI water Hydroxyethyl cellulose	99.90	99.80
Amla branch extract	-	0.1
Liquid germall™ plus	0.1	0.1

Table C Physicochemical properties of base and PE gels at initial and after 7 cycles of heating-cooling cycle

Condition	Physicochemical properties	Base gel	PE gel
At initial	pH	6.40 ± 0.10	5.10 ± 0.10
	Viscosity (cps)	1,796.67 ± 4.16	3,425.33 ± 6.11
After heating-cooling cycle	pH	6.30 ± 0.10	4.84 ± 0.03
	Viscosity (cps)	1,782.00 ± 2.00	3,280.00 ± 6.00

Table D Skin measurement in clinical anti-skin aging efficacy

Parameters	Mild aging		Moderate aging	
	Base gel	**PE gel**	**Base gel**	**PE gel**
Skin color (ITA°)				
Baseline	31.13 ± 2.20	31.07 ± 2.40	22.59 ± 2.97	22.94 ± 2.88
14 d of application	31.80 ± 2.11	32.04 ± 2.32	24.09 ± 3.42	24.51 ± 3.00
28 d of application	31.47 ± 1.95	31.41 ± 2.01	24.07 ± 3.41	24.81 ± 3.00
42 d of application	31.48 ± 1.79	31.61 ± 2.16	24.98 ± 3.37	25.13 ± 3.07
56 d of application	31.18 ± 1.97	31.61 ± 2.15	24.68 ± 3.25	25.82 ± 3.26
70 d of application	30.99 ± 2.02	32.40 ± 2.10	23.87 ± 2.49	25.53 ± 3.06
84 d of application	31.71 ± 2.31	33.07 ± 2.15	23.81 ± 2.65	26.15 ± 3.06
Skin pigment				
Baseline	227.71 ± 17.83	231.35 ± 20.94	255.79 ± 19.35	265.67 ± 22.01
14 d of application	225.15 ± 17.81	232.79 ± 22.88	244.19 ± 19.10	245.32 ± 17.77
28 d of application	226.44 ± 15.98	227.44 ± 20.19	250.08 ± 22.11	244.51 ± 20.71
42 d of application	227.23 ± 15.74	228.90 ± 19.70	239.64 ± 20.48	250.63 ± 19.51
56 d of application	221.31 ± 17.34	226.07 ± 21.24	237.54 ± 18.87	240.79 ± 17.93
70 d of application	222.39 ± 17.50	217.69 ± 20.03	242.80 ± 16.01	232.71 ± 17.71
84 d of application	220.34 ± 18.55	209.15 ± 18.38	246.63 ± 15.83	226.83 ± 17.69
Skin elasticity				
Baseline	478.30 ± 35.98	554.23 ± 40.37	1207.27 ± 252.44	1338.93 ± 281.24
14 d of application	465.43 ± 25.10	502.30 ± 34.00	1192.63 ± 259.02	1211.73 ± 272.79
28 d of application	490.33 ± 41.57	479.97 ± 40.81	1238.20 ± 258.55	1180.17 ± 265.26
42 d of application	515.90 ± 33.49	507.13 ± 41.95	1246.43 ± 289.39	1181.17 ± 274.81
56 d of application	497.07 ± 33.12	501.90 ± 40.36	1283.33 ± 254.02	1191.33 ± 259.39
70 d of application	523.13 ± 33.68	482.37 ± 30.18	1262.33 ± 260.60	1077.33 ± 215.85
84 d of application	514.87 ± 42.96	439.13 ± 28.28	1175.70 ± 255.46	1002.13 ± 175.73
Skin wrinkle reduction				
Baseline	38.33 ± 1.95	38.08 ± 1.04	37.27 ± 0.50	39.34 ± 1.32
14 d of application	36.77 ± 1.69	37.45 ± 1.38	37.38 ± 0.88	37.67 ± 1.11
28 d of application	37.60 ± 1.57	36.19 ± 1.42	37.72 ± 0.78	37.49 ± 1.06
42 d of application	36.65 ± 1.34	35.89 ± 1.31	38.18 ± 0.98	38.30 ± 1.21
56 d of application	36.19 ± 0.93	37.07 ± 1.11	37.33 ± 0.94	36.76 ± 1.30
70 d of application	37.16 ± 1.21	36.10 ± 0.91	37.30 ± 0.72	37.76 ± 1.18
84 d of application	36.97 ± 1.46	34.96 ± 0.92	35.80 ± 0.76	36.40 ± 1.27
Skin hydration				
Baseline	63.06 ± 2.63	62.43 ± 2.59	61.22 ± 2.52	61.09 ± 2.51
14 d of application	63.85 ± 3.03	64.34 ± 2.68	64.22 ± 2.09	65.72 ± 2.39
28 d of application	64.40 ± 2.74	65.33 ± 2.71	66.61 ± 1.85	67.75 ± 1.81
42 d of application	65.29 ± 3.39	65.61 ± 2.97	66.47 ± 2.14	67.10 ± 1.67
56 d of application	67.05 ± 2.60	67.89 ± 2.49	66.79 ± 1.65	67.70 ± 1.88
70 d of application	66.64 ± 2.35	68.72 ± 1.96	66.80 ± 1.63	68.04 ± 1.93
84 d of application	67.78 ± 2.43	70.29 ± 1.88	65.99 ± 1.78	68.28 ± 1.90

References

1. Krishnaveni M, Mirunalini S. Chemopreventive efficacy of *Phyllanthus emblica* L.(amla) fruit extract on 7, 12-dimethylbenz (a) anthracene induced oral carcinogenesis–A dose–response study. *Environ Toxicol Pharmacol.* 2012;34:801-810.
2. Vaithiyanathan V, Mirunalini S. Chemo preventive potential of fruit juice of *Phyllanthus emblica* Linn. (amla) against mammary cancer by altering oxidant/antioxidant status, lipid profile levels and estrogen/progesterone receptor status in female Sprague–Dawley rats. *Biomed Prev Nutr.* 2013;3:357-366.

3. Rosarin FS, Arulmozhi V, Nagarajan S, Mirunalini S. Antiproliferative effect of silver nanoparticles synthesized using amla on Hep2 cell line. *Asian Pac J Trop Med.* 2013;6:1-10.
4. De A, De A, Papasian C, et al. *Emblica officinalis* extract induces autophagy and inhibits human ovarian cancer cell proliferation, angiogenesis, growth of mouse xenograft tumors. *PloS ONE.* 2013;8:e72748.
5. Vadde R, Radhakrishnan S, Eranda Karunathilake Kurundu H, Reddivari L, Vanamala JKP. Indian gooseberry (*Emblica officinalis* Gaertn.) suppresses cell proliferation and induces apoptosis in human colon cancer stem cells independent of p53 status via suppression of c-Myc and cyclin D1. *J Funct Foods.* 2016;25:267-278.
6. Kasabri V, Flatt P, Abdel-Wahab Y. *Emblica officinalis* stimulates the secretion and action of insulin and inhibits starch digestion and protein glycation *in vitro*. *Eur J Med Plants.* 2014;4:753-770.
7. Muthuraman A, Sood S, Singla SK. The antiinflammatory potential of phenolic compounds from *Emblica officinalis* L. in rat. *Inflammopharmacology.* 2011;19:327-334.
8. Rao TP, Okamoto T, Akita N, Hayashi T, Kato-Yasuda N, Suzuki K. Amla (*Emblica officinalis* Gaertn.) extract inhibits lipopolysaccharide-induced procoagulant and pro-inflammatory factors in cultured vascular endothelial cells. *Br J Nutr.* 2013;110:2201-2206.
9. Middha SK, Goyal AK, Lokesh P, et al. Toxicological evaluation of *Emblica officinalis* fruit extract and its anti-inflammatory and free radical scavenging properties. *Pharmacogn Mag.* 2015;11:S427.
10. Saeed S, Tariq P. Antimicrobial activities of *Emblica officinalis* and *Coriandrum sativum* against gram positive bacteria and *Candida albicans*. *Pak J Bot.* 2007;39:913-917.
11. Mehrotra S, Srivastava AK. Comparative antimicrobial activities of neem, amla, aloe, Assam tea and clove extracts against *Vibrio cholerae*, *Staphylococcus aureus* and *Pseudomonas aeruginosa*. *J Med Plant Res.* 2010;4:2393-2398.
12. Al-Rehaily AJ, Al-Howiriny TA, Al-Sohaibani MO, Rafatullah S. Gastroprotective effects of 'Amla' *Emblica officinalis* on *in vivo* test models in rats. *Phytomedicine.* 2002;9:515-522.
13. Sairam K, Rao CV, Babu MD, Kumar KV, Agrawal V, Goel RK. Antiulcerogenic effect of methanolic extract of *Emblica officinalis*: an experimental study. *J Ethnopharmacol.* 2002;82:1-9.
14. Mehmood MH, Rehman A, Rehman Nu, Gilani AH. Studies on prokinetic, laxative and spasmodic activities of *Phyllanthus emblica* in experimental animals. *Phytother Res.* 2013;27:1054-1060.
15. Rege NN, Thatte UM, Dahanukar SA. Adaptogenic properties of six rasayana herbs used in Ayurvedic medicine. *Phytother Res.* 1999;13:275-291.
16. Yokozawa T, Kim HY, Kim HJ, Okubo T, Chu D-C, Juneja LR. Amla (*Emblica officinalis* Gaertn.) prevents dyslipidaemia and oxidative stress in the ageing process. *Br J Nutr.* 2007;97:1187-1195.
17. Fujii T, Wakaizumi M, Ikami T, Saito M. Amla (*Emblica officinalis* Gaertn.) extract promotes procollagen production and inhibits matrix metalloproteinase-1 in human skin fibroblasts. *J Ethnopharmacol.* 2008;119:53-57.
18. Pathak P, Prasad BRG, Murthy NA, Hegde SN. The effect of *Emblica officinalis* diet on lifespan, sexual behavior, and fitness characters in *Drosophila melanogaster*. *Ayu.* 2011;32:279-284.

19. Rawal S, Singh P, Gupta A, Mohanty S. Dietary intake of *Curcuma longa* and *Emblica officinalis* increases life span in *Drosophila melanogaster*. *BioMed Res Int.* 2014;2014:910290.