

Ksharagada: An Ayurvedic Formulation with Emphasis on Antioxidant Potential and Mechanistic Insights – A Narrative Review

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Abstract: Background: Ksharagada is the formulation explained by bhihatrayi's like in Charaka Samhita and the Susruta Samhita for the treatment of various conditions related to visha. Classically it is indicated in Shotha, pandu, twakaroga gulma etc. This formulation is explained under agada tantra i.e toxicology which may help to get rid of toxins and supporting body to normalize agni by amapachana and bringing vitiated dosha's to normalcy. Most of the drugs in ksharagada are having Katu and Tikta Rasa, Ushna Veerya, and Laghu Ruksha Gunatmaka. Antioxidant potential is defined as the ability to neutralize oxygen free radicals that are generated in excess due to oxidative stress. Oxidative stress happens in body due to imbalance of antioxidant defences and the production of reactive oxygen species which can causes a lot of diseases by altering lipid peroxidation, protein denaturation, DNA damage, mitochondrial dysfunction, and cell death. Chemical constituents of Ksharagada ingredients are polyphenols, flavonoids, alkaloids, tannins, curcumin, berberine, piperine, gingerols, glycyrrhizic acid, and sesquiterpenes etc act as Anti-inflammatory, Antioxidant, Hepatoprotective, Antimicrobial, Immunomodulatory. By the virtue of these actions the preparation may help to reduce inflammatory cascade by directly scavenging free radicals, reducing lipid peroxidation, and activating cellular defence pathways, hence reduce inflammation and oxidative stress. The present paper is as attempt to understand antioxidant action of Ksharagada with special reference with its chemical constituents.

Keywords: Ksharagada, Phytochemical studies, Antioxidant.

INTRODUCTION

Antioxidant potential is the ability to neutralize oxygen free radicals that are generated in excess due to environmental influences. To prevent the oxidative stress, bodies defence mechanism is essential.¹ Oxidative stress is an imbalance in the production of reactive oxygen species and ability to neutralize them and finally to repair damage. Physiologically, cells are maintained in a reducing environment, provided by endogenous antioxidants or antioxidant enzymes. Increased levels of oxidative stress have consequences such as lipid, protein, and nucleic acid modifications, which ultimately lead to a worsening of mitochondrial function and cell death.^{2,3} All this led to cellular dysfunctions and many diseases like neurodegenerative diseases like Alzheimer's and Parkinson's disease, atherosclerosis, obesity etc.^{2,3,4,5}

Ayurveda being ancient science of life, explains various formulations designed to reduce oxidative stress like Ksharagada. One among 8 branches of ayurveda is Agada Tantra which especially deals with this by neutralizing toxins, enhancing elimination pathways, and reducing oxidative stress by virtue of its Antioxidant properties. Agada Tantra is the branch of Ayurveda which deals with the management of poisonous bites and toxic combination.⁶ It is also named as Visha chikitsa. As per the Ayurvedic treaties, the Dravya which causes Vishaad (depression) is known as Visha

for the treatment of conditions manifested by poison such as. Shotha (inflammation), Gulma (bloating), Twakdosa (skin diseases), Pandu (anaemia) and also in Krimi Roga.⁷ The drugs in the formulation act by on the basis of Rasa, Guna, Veerya, Vipaka and Prabhava which explains the probable mode of drug action.⁸ The ingredients of Ksharagada having antioxidant, antibacterial and hepatoprotective action.

Phytochemical studies of Ksharagada showed various actions like antiallergic, antimicrobial, antileukemic, anti-inflammatory, antifungal, antioxidant, antibacterial and anticarcinogenic agents were found, demonstrating the drug's therapeutic efficacy.^{9,10,11,12,13} These findings suggest that the traditional anti-toxic claims of Ksharagad may be closely linked to its ability to modulate oxidative stress, scavenge free radicals, and regulate inflammatory pathways. Present paper is as attempt to critically review Ksharagad with emphasis on its antioxidant potential.

Aim & Objectives:

1. To study the pharmacological and therapeutic action of Ksharagada.
2. To evaluate the antioxidant potential of Ksharagada

Classical review of Ksharagada

Ksharagad is a classical Ayurvedic formulation described in Charaka Samhita, Sushruta Samhita. The formulation is traditionally prepared using an kshara,

*Ksharagada is one of the formulations described by Acharya Charaka and Acharya Sushruta. It is indicated

along with selected medicinal herbs possessing visha hara, shothahara, and rasayana attributes.

RESULTS

Ingredients and pharmacodynamic properties of Ksharagada:

S N	Drug	Botanical Name	Rasa	Guna	Veerya	Vipaka	Karma	Doshaghanta
1	Palasha ¹⁴	Butea monosperma Lam.	Katu, Tikta, Kashaya	Laghu, Ruksha	Ushna	Katu	Krimighna, Kushthaghn a, Vishaghna	Kapha-Vatashamaka
2	Gairik	Red ochre	Madhura, Kashaya	Snigdha	Sheeta	Madhura	Vishaghna	Pittashamaka
3	Haridra ¹⁵	Curcuma longa Linn.	Tikta, Katu	Ruksha, Laghu	Ushna	Katu	Krimighna, Kushthaghn a, Vishaghna	KaphaVatasha maka Tikta Rasa-Pittashamaka
4	Daruharidr a ¹⁶	Berberis aristata DC	Tikta, Kashaya	Laghu, Ruksha	Ushna	Katu	Shothahara, Kandunasha ka	Kapha-Pittashamaka
5	Surasmanj ari ¹⁷	Ocimum sanctum Linn.	Katu, Tikta	Laghu, Ruksha	Ushna	Katu	Shothahara, Krimighna, Vishaghna	Kapha-Vatashamaka
6	Madhuka ¹⁸	Glycyrrhiza glabra Linn.	Madhura	Guru, Snigdha	Sheeta	Madhura	Shothahara, Kandughna	Vata-Pittashamaka
7	Laksha ¹⁹	Laccifer lacca	Katu, Tikta	Laghu, Snigdha	Ushna	Katu	Kushthaghn a	Kapha-vatashamaka
8	Saindhav ²⁰	Rock salt	Lavana, Madhura	Snigdha, Tikshna, Sukshma	Sheeta	Madhura	Vrushya, Deepaniya	Tridoshhara
9	Jatamansi ²¹	Nardostachys jatamansi DC	Tikta, Kashaya, Madhura	Laghu, Snigdha	Sheeta	Katu	Medhya, Balya, Kushthaghn aa	Tridoshahara
10	Harenu ²²	Vitex agnus	Katu, Tikta	Laghu	Sheeta	Katu	Deepana, Pachana, Medhya, Vishaghna	Kapha-Vatanashaka
11	Hingu ²³	Ferula narthex Boiss.	Katu	Laghu, Snigdha, Teekshna	Ushna	Katu	Deepana, Pachana, Rochana, Krimighna	Kapha-Vatashamaka
12	Shweta Sariva ²⁴	Hemidesmus indicus R. Br.	Madhura	Guru, Snigdha	Sheeta	Madhura	Kushthaghn a, Vishaghna, Rochaka	Tridoshahara
13	Krushna Sariva ²⁵	Ichnocarpus frutescens	Madhura	Snigdha, Guru	Sheeta	Madhura	Kushthaghn a, Vishamjwar anashaka	Tridoshahara
14	Kushtha ²⁶	Saussurea lappa C.B Clarke	Tikta, Katu, Madhura	Laghu, Ruksha, Teekshna	Ushna	Katu	Kushthaghn a, Jwaraghna,	Kapha-Vatashamaka
15	Shunthi ²⁷	Zingiber officinale Rosc.	Katu	Laghu, Snigdha	Ushna	Madhura	Shothahara, Deepana, Pachana, Vrushya	Kapha-Vatashamaka

16	Maricha ²⁸	Piper nigrum Linn.	Katu	Laghu, Teekshna	Ushna	Katu	Deepana, pachana, Krimighna, Kushthagha	Kapha-vatashamaka
17	Pippali ²⁹	Piper longum Linn.	Katu	Laghu, Snigdha, Teekshna	Anushn asheeta	Madhura	Krimighna, Kushthagha	Kapha-vatashamaka
18	Bahlika ³⁰	Crocus sativus Linn.	Katu, Tikta	Snigdha	Ushna	Katu	Shothahara, Deepana, Pachana	Tridosahara

Collect taruna Palasha Kshara and mixed with water in a 1:6 ratio, then swirled well. This combination is left alone for two hours so that it can settle to the bottom of the glass jar. A double-folded cloth is used to filter the mixture, and then it is put into a measuring jar. This filtering process was done 21 times, and Ksharodka was eventually gathered and weighed. A steel pot was used to boil Ksharodaka. After 30 minutes of boiling, add Sukshma churna of all the dravya's and mixed well. Stir the mixture until it became thick. After cooling down on its own, collect the Ksharagada.

The therapeutic action of Ksharagada can be explained through the concept of rasapanchaka. Most of the ingredients are Katu (pungent), Tikta (bitter) rasapradhana, the Guna's are Laghu (light), Tikshna (sharp), Ruksha (dry). They have ushna virya and katu vipaka. The collective action of the ingredients of ksharaagada are Visha hara, Agni Deepana, Ama pachana, Shothahara and Krimighna. By virtue of these actions, it will help to reduce oxidative stress by neutralization and elimination of free radicals. By these properties the drugs of Ksharagada may act on various signs & symptoms of Visha.

Chemical composition of Ingredients of Ksharagada

Sr. no.	Drug	Chemical Composition
1	Palasha ³¹	Kino acid, tannic acid, gallic acid, two flavonoids butrin & isobutrin
3	Haridra ³²	Curcumene, Curcumenone, Curcone, Curdione, Cineole, Curzerenone, Epiprocucumenol, Eugenol, Camphene, Camphor, Bornel
4	Daruharidra ³³	Berberine, berbamine, oxycanthene, epiberberine, palmatine, dehydrocaroline, columbamine etc.
5	Surasmanjari ³⁴	Bornyl acetate, cardinene, camphene, Camphor, Carvacrol, b- Carryophellene, Eugenol, palmitic acid, gallic acid methyl ether, humelene, Methyl chavicol
6	Madhuka ³⁵	Glycyrrhine, prenylated baurone, licoagron, isoflavone, liqcomarin, glyzaglabrin, quercetin, kaempferol, stragalon, liquoric acid, glabrotide, deoxoglabrotide, glycyrrhizic acid, liconicone, blabridin, liquirazid, liquiritin, glabranine
7	Laksha ³⁶	Resin, dye, wax, albuminous matter, mineral matter and water, resinolannols of aleuritic acid, erythrolaccin, laconic acid.
9	Jatamansi ³⁷	Actinidine, Carotene, Aristolens, Calarence, elemol, Droaristolene, B-eudesmol, Jatamols, Jatamansic acid, Jatamansone, Nardol, Nardostachonol, Nardostachone, Patchouli, Virolin, Angelivin, Jatamansin, Jatamansinol
10	Harenu ³⁸	Phenol, dulcitol, alkaloid-vitricine, B-sitosterol, camphene, A & B- Pinenes, Angoside, Acunbin, casticin, artemetin, orientin.
11	Hingu ³⁹	Ferulic acid, coumarins, sesquiterpene, terpenoids, galactose, 1-arabinose, rhamnose, glucuronic acid
12	Sariva ⁴⁰	Hyperoside, rutin, desinine, hexatriacontane, hemidesminine, hemidesmin-1 & hemidesmin-2
13	Kushtha ⁴¹	Essential oil, costol, taraxas- terol, constunolide, Dehydro constuhactone, alpha-Cyclocostunolide, sitosterol, Sesquiterpenes, isodihydrocostuslactone, costol-lactone
14	Shunthi ⁴²	Curumene, B-D- Curcumene, B-Bourbornene, d- Borneal, Citral, D- Camphene, Citronellol, Geraniol, Gingerol, a-&b-Zingiberenes, Zingiberol, Zingerone, Gingerols
15	Maricha ⁴³	Piperine, Piperethine, Piperolein A & B, feruperine, Dihydroferuperine, Citronellol, Cryptone, Dihydrocarveol, Piperonal
16	Pippali ⁴⁴	Piperine, Piperlongumine, Piperlonguminine, Pipernonaline, Piperundecalidine, Pipericide, Sesamin
17	Bahlika ⁴⁵	Terpenes, terpene alcohols, esters, crocin, picrocrocin, crocetin, carotenoids thiamine

RESEARCH ARTICLE DISCUSSION

Palasha exhibit liver protective activity by decreasing the levels of serum alanine phosphatase and alkaline transaminase also by enhancing the rate of collagen synthesis & cellular proliferation it helps in wound healing. 46 Volatile oils & curcumene of haridra shows potent anti-inflammatory effects by inhibiting prostaglandins synthesis. It also having anti-oxidant, hepatoprotective activity. 47 Daruharidra shows anti-allergic & anti-inflammatory property, it has anti-oxidant, antipyretic, anti-bacterial, anti-hepatotoxic properties. 48 Eugenol and carvacrol present in Tulsi shows antimicrobial activity, anti-inflammatory and hepatoprotective activity. 49 Chemical composition of Madhuka like licoagron, glycyrrhine, licoamarin, glyzaglabrin, liquoric acid, glycyrrhizic acid, liconicone etc acts as a hepatoprotective also have properties like antioxidant, antimicrobial, anti-inflammatory. 50 Laksha shows anti-inflammatory, hepatoprotective property. 51 Saindhav supports disposing of toxic minerals and refined salt store by invigorating circulation system. 52 Jatamansi is hepato-protective, neuroprotective. 53

Hingu is very powerful anti-oxidant and protects body from the effect of various free radicals. Also having anti-inflammatory, anti-viral, antibiotic action. 54 Sariva contains large amounts of flavonoids and phenolic compounds, hence shows high antioxidant and free radical scavenging activities. 55 Kushtha contains sesquiterpene lactones which exhibits anti-inflammatory, antiulcer, anti-cancer and hepatoprotective activities. 56 Zingiber officinale contains zingerol showing immuno-modulatory, anti-tumorigenic, anti-inflammatory, anti-apoptic, anti-hyperglycaemic actions. 57 Maricha controls inflammations. 58 Pippali have properties like anti allergic, antipyretic, analgesic and anti-inflammatory. 59 Bahlika is rich source of riboflavin and thiamine. It is a mild stimulant and is consider as promoter of immunity. 60

The phytochemical constituents of Ksharagada mostly polyphenols, flavonoids, alkaloids, tannins, and terpenoids contribute to antioxidant defence via Direct Free Radical Scavenging activity by Neutralization of superoxide radicals, Scavenging hydroxyl radicals, Reduction of hydrogen peroxide (H_2O_2), Prevention of lipid peroxidation in cell membranes. Phenolic compounds donate hydrogen atoms or electrons to stabilize reactive species. For example, Antioxidant activity of butea monosperma flowers was studied in vitro models such as the radical scavenging activity using 2, 2 diphenyl 1 picrylhydrazyl (DPPH) assay, reducing power assay. Nitric oxide scavenging activity and antioxidant capacity. 61

Several constituents of ksharagada like curcumin and berberine are known to activate the Nrf2 signalling pathway, leading to transcription of antioxidant response

element -regulated genes. This results in Enhanced

cellular detoxification, Increased production of phase II antioxidant enzymes and Cytoprotection against oxidative injury. 62 The detoxifying action of Ksharagada can be mechanistically correlated with its antioxidant potential. By scavenging reactive oxygen species, stabilizing cellular membranes, and modulating inflammatory signalling pathways, the formulation may reduce oxidative damage associated with toxic exposure and chronic inflammation.

The liver plays a crucial role in Detoxification which corresponds to the Ayurvedic concept of vishahara. Ingredients such as Katuki, Haridra, Daruharidra, and Triphala components demonstrate strong hepatoprotective activity and detoxification activity. 63 Certain drugs like shunti, maricha etc reduce free oxygen radicals by regulating metabolic pathways like regulating Lipid metabolism. Immunomodulatory Effects of certain drugs in formulation helps in Macrophage activity, Cytokine regulation indirectly contributing to reduce oxidative stress.

Conclusion:

The formulation, as described in the Charaka Samhita and Sushruta Samhita of ayurvedic classics, act as Visha hara, Agni Deepaka, amapachaka. The ingredients of ksharagada contains polyphenols, flavonoids, alkaloids, terpenoids, curcumin, berberine, piperine, and gingerols etc which are antioxidant, anti-inflammatory, hepatoprotective, and immunomodulatory. By virtue of their action they exhibit scavenge free radicals, inhibit lipid peroxidation, stabilise cell membranes, and activate antioxidant pathways as a potent anti-oxidant action. Hence Ksharagada may promote detoxification, reduce inflammation and do immunomodulation.

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