Review Article

Narrative review of guggulu formulations of ayurveda reflecting their percentage of guggulu, pharmaceutics and pharmacology

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ABSTRACT

Guggulu is known for its health benefits and therapeutic effects since ancient times. Its bitter taste, and non-palatability in liquid form resulted in discovery of new type of formulation called guggulu kalpana. Guggulu is oleo gum resin of the plant Commiphora wightii hence it acts as a binder when formulated as a tablet along with other ingredients. In recent times a lot of emphasis is being given to natural excipients over synthetic as they have no side effects and possess therapeutic value. This review article focuses on critical aspects of Ayurvedic guggulu formulations in view of the proportion of guggulu along with other ingredients for therapeutic efficacy as well as an excipient (specifically as a binder). It also emphasizes on the pharmaceutics of Guggulu formulations as a speciality of Ayurveda as well as its pharmacology.

1. Introduction

Ayurvedic medicine involves use of various types of formulations. The formulations include basic formulations [juice, decoction, paste, powders, cold and hot infusions], and advance formulations like medicated ghee, medicated oil, semisolid avaleha preparations, fermentation products of acidic and alcoholic nature, pills of various sizes and guggulu formulations [specialised preparations of oleo gum resin of guggulu], and many more.

1.1. Various types of formulations in Ayurvedic system of medicine

The basic formulations include herbal fresh juice, decoction, paste, cold infusion, hot infusion. Further formulations are modified and advanced versions of these basic dosage forms. The need for modifications was observed when these basic formulations missed the mark to fulfil criteria like shelf life, palatability and stability. Most patients cannot prepare drugs freshly due to practical issues. Palatability issues arise in infants and pregnant females due to the smell and taste of the medicine. The shelf life of these dosage forms is only couple of hours after they are prepared i.e., they become unstable for consumption as microorganisms grow in them and they get contaminated due to high moisture content. If they are preserved, the adverse effects of preservation come into picture.

Therefore, to overcome and to fulfil the above-mentioned criteria, pill formulations emerged. The preparation of pills requires a binding agent like sugar, jaggery, gum resin of commiphora wightii (guggulu) to bind the ingredients and for uniform shape of guti-vati. These are the natural binders.
<table>
<thead>
<tr>
<th>S.No.</th>
<th>Kalpa</th>
<th>Dose according to classical ref</th>
<th>Percentage of guggulu</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Sinhanad guggulu²</td>
<td>2-3 gm in divided dose</td>
<td>11.11% RHEUMATOID ARTHRITIS, SKIN DISEASE, GOUT, TUMOUR, PAINFUL CONDITION, REJUVENATION, ETC (ANUPAN-GHRUTA, TAILA, MANSARASA, SHAALI)</td>
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<td>2.</td>
<td>Gokshuradi guggulu³</td>
<td>[1 shaan=3gm] 3gm divided dose.</td>
<td>12.5% DIABETES, BURNING SENSATION ON URINATION (MUTRARKRUCHRA), MENORRHAGIA (PRAZAR), ANURIA (MUTRAGHATA), GOUT (VATARAKTA), RENAL CALCULI (ASHMARI)</td>
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<td>3.</td>
<td>Amrutaakhya guggulu⁴</td>
<td>2-3 gm</td>
<td>13.7% GOUT, SKIN DISORDER (KUSHTHA), TREATMENT OF WOUND (DUSTAVRANA), DIABETES (PRAZMA), RHEUMATOID ARTHRITIS (AAMVATA), FISTUL (BHAGANDAR), PILONIDAL SINUS (NAADIVRANA)</td>
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<tr>
<td>4.</td>
<td>Panchatiktak guggulu⁵</td>
<td>6-12 gm divided dose.</td>
<td>14.2% SKIN DISORDERS INVOLVING TOXICITY OR RASHES, ANTI-TOXIC ACTIVITY, VATA RELATED DISORDERS (VATAVYADHI), TUMOUR (GULMA), DIABETES (MEHA), ANEMIA (PANDU)</td>
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<td>5.</td>
<td>Punarnava guggulu⁶</td>
<td>2-3 gm divided dose.</td>
<td>16.6% SKIN DISORDER (TWACHAROGA), SWELLING (SHOTHA), ANEMIA (PANDU), OBESITY (STHAULYA), KAPHAROGA.</td>
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<tr>
<td>6.</td>
<td>Vatari guggulu⁷</td>
<td>early in morning with warm water for a month 2-3gm divided dose.</td>
<td>16.6% VATA VYADHI, PAINFUL CONDITIONS LIKE SCIATICA, RA, GOUT, BURNING SENSATION AT EXTREMITIES.</td>
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<td>7.</td>
<td>Loha guggulu⁸</td>
<td>1 karsha = 12 gm</td>
<td>17.6% REJUVENATOR.</td>
<td></td>
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<tr>
<td>8.</td>
<td>Kaishor guggulu⁹</td>
<td>3 gm</td>
<td>18.13% GOUT (VATARAKTA), SKIN DISORDER (KUSHTHA), WOUND (VRANA), DIABETIC WOUNDS (PRAZMA PITIKA), DIABETES (PRAZMA), ASCITIS (UDAR), ANEMIA (PANDU), REJUVENATION (RASYANA), IMPROVES SKIN HEALTH, EYE DISEASES (NETRAROGA), VRANAKUSHTHAGHNA (TO BE CONSUMED WITH KHADIR KWATHA).</td>
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<tr>
<td>9.</td>
<td>Chandraprabha¹⁰</td>
<td>125mg to 500 mg</td>
<td>20.51% DISORDERS OF TEETH (DANTAROGA), EYE DISORDER (NETRAROGA), AARTAVADUSHI, SHUKRADUSHI, MANDAGNI, ANOREXIA (ARUCHI), DYSPEA (SHWAS), COUGH (KAAS), SKIN DISORDERS (KUSHTHA), DIABETES (PRAZMA), BURNING SENSATION ON URINATION (MUTRARKRUCHRA), ANURIA (MUTRAGHATA), RENAL CALCULI (ASHMARI), TUMOUR (GRANTHI), PAIN IN LOWER BACK (KATISHOOLA), ASCITES (UDAR), FISTULA (BHAGANDAR), REJUVENATION (RASYANA).</td>
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<td>10.</td>
<td>Amruta guggulu¹¹</td>
<td>3 gm</td>
<td>21.7% GOUT (VATARAKTA), SKIN DISORDER (KUSHTHA), HAEMORRHIOIDS (ARSHA), WOUND (DUSHTAVRANA), DIABETES (PRAZMA), RHEUMATOID ARTHRITIS (AAMVATA), FISTULA (BHAGANDAR).</td>
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<tr>
<td>11.</td>
<td>Amrutadi guggulu¹²</td>
<td>3 gm</td>
<td>22.22% DIABETIC WOUND (PRAMEHAPIDIKHA), FISTULA (BHAGANDAR), OBESITY (STHAULYA).</td>
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<td>12.</td>
<td>Mahayograj guggulu¹³ (sha)</td>
<td>3 gm</td>
<td>25.86% VATA DISORDERS (VATAVYADHI), SKIN DISORDERS (KUSHTHA), ARSHA, DIABETES (PRAZMA), FISTULA (BHAGANDAR), TUBERCULOSIS (KSHAYA), EPILEPSY (APASMAR), ANOREXIA (ARUCHI), ANEMIA (PANDU).</td>
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<td>13.</td>
<td>Loha guggulu¹⁴</td>
<td>1 karsha= 12gm with ushnodaka</td>
<td>33.3% ANEMIA (PANDU), JAUNDICE (KAMALA)</td>
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<table>
<thead>
<tr>
<th>Table 1 continued</th>
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<tbody>
<tr>
<td>14. Yograj guggulu^{15}</td>
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<tr>
<td>15. Tryushnadi guggulu^{16}</td>
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<tr>
<td>16. Kanchanar guggulu^{17}</td>
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<td>17. Navaka guggulu^{18}</td>
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<tr>
<td>18. Abha guggulu^{19}</td>
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<tr>
<td>19. Vidangadi guggulu^{20}</td>
</tr>
<tr>
<td>20. Amruta guggulu^{21}</td>
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<tr>
<td>22. Swayambhuuakhya guggulu^{23}</td>
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<tr>
<td>23. Aabha guggulu^{24}</td>
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<tr>
<td>24. Laksha guggulu</td>
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<tr>
<td>25. Chitrakadi guggulu</td>
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<tr>
<td>26. Panchamrut Loha Guggulu^{25}</td>
</tr>
<tr>
<td>27. Trayodashanga guggulu^{26}</td>
</tr>
<tr>
<td>28. Aditya Paka guggulu^{27}</td>
</tr>
<tr>
<td>29. Navakarshik Guggulu^{28}</td>
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<tr>
<td>30. Ekvinshti guggulu^{29}</td>
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<tr>
<td>31. Triphala guggulu^{30}</td>
</tr>
<tr>
<td>32. Saptang guggulu^{31}</td>
</tr>
<tr>
<td>33. Saptavinshati guggulu^{32}</td>
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<tr>
<td>34. Rasna Guggulu</td>
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</table>
Jaggery and sugar being part of diet are specifically used for palatability and vata alleviating action and soothing action in throat, making it easy for consumption. The shelf life of the vati prepared using jaggery is less thus very few formulations like ‘bahushala guda’, ‘marichadi gutika’, ‘suranavatak’ etc are prepared using jaggery and sugar. The tablets such as ‘vyoshadi vataka’ made using jaggery as a binder are hygroscopic, and they may stick to one another when packed. Hence there are challenges in large scale manufacturing of such tablets. Research and development are needed to convert these into marketable products.

In modern pharmaceutical practices chemical binding agents are used which are inert and their purposes vary, like used as binders, lubricants, disintegrants etc. On the contrary Guggulu formulations are special; as Guggulu is of medicinal value, it is good as a binding agent, and possesses various properties to eliminate diseases. Considering the Ayurvedic properties and actions of guggulu it has been primarily chosen as a gum for binding the tablets. It has a wide range of usefulness in indigenous medicine. It is astringent and antiseptic and acts as a bitter, promoter of appetite, and relieves flatulence when taken internally. It acts as a diaphoretic, expectorant, diuretic, uterine stimulant. Inhalation of the fumes from burnt guggulu is recommended as it is praised as ‘Devadhupa’.

2. Speciality of Guggulu formulations

Guggulu is the oily-gummy resinous substance extracted from the bark of Commiphora wightii.

As per the general guideline the quantity of Guggulu is 50 % and that of other ingredients is 50 %. In various guggulu kalpana like trayodashang guggulu and kanchnar guggulu the quantity of guggulu was 50 percent, however while we review the ancient literature of Ayurveda it was evident that in various other guggulu formulations [eg Gokshuradi guggulu, Vatari Guggulu] the quantity of guggulu is not 50 %. This has been reviewed and compiled in Table 1. The table mentions only main indications; however, the drugs are also indicated in medical conditions only after complete assessment by an Ayurvedic physician.

Fresh guggulu [Nava Guggulu] is supposed to be the one collected and used within a year. Mature Guggulu [Purana guggulu] is the one used after storing for a year or more. Fresh one should be used where nourishing or anabolic and aphrodisiac function is expected and mature guggulu should be used where intense catabolic action is expected. Critical analysis of the percentage of guggulu, used in preparation of guggulu formulations is carried out here.

As per agryasangraha [best drug index] of the Ayurvedic classical text ‘Ashtangahruday’, Guggulu is the primarily most important drug for treatment of ailments involving fat tissue [Meda dhatu].

The dose adjustment of the formulation is dependent on many factors including strength of the patient, his age, his body constitution, region, season. However classical dose must be taken into consideration while treatment.

In some classical formulations, there are many indications, here not only dose but time of drug administration [aushadhi sevan kala] also matters. A drug can be effectively used for many conditions by correct choice of drug delivery time, such as – early in morning [for rejuvenation], before lunch [for vyana vayu disorders] etc.

From the above list it is clear that the quantity of guggulu in these guggulu formulations varies with respect to other ingredients, this may be due to the expected synergistic activity of the formulation and role of guggulu in it. Ayurvedic formulations are complex drugs based on the principles of synergism and antagonism in order to achieve desired effect of the formulation. To avoid the adverse drug reactions due to its extreme pitta aggravating action; processing of guggulu is carried out by dissolving it in liquid media like decoction of Adhatoda vasica, decoction of triphala [Terminalia chebula, Terminalia belerica. Emblica officinalis], or cow milk, followed by straining and
condensation which is known as purification.\textsuperscript{34}

When the quantity of guggulu is 50% or more, it is used for its own therapeutic effects predominantly synergistically with other drugs whereas when this percentage is lesser [eg – 12.5% guggulu in Gokshuradi Guggulu], it may have been added for its yogavahi action [carrier/ supporting accompanying medicament]. The mechanism of action of the guggulu formulation is influenced by the other drugs present in it, this process in modern medicines/pharmaceutics is called synergistic action. Considering this process, the selection of guggulu i.e., fresh and mature should be done according to the effects expected such as anabolism or catabolism respectively. Following are some examples of most commonly used formulations of guggulu and the critical analysis of their composition and action with few examples below.

2.1. Gokshuradi guggulu\textsuperscript{3}

This is one of the most widely used formulation of guggulu in disorders of urinary system, including renal calculi. This formulation contains guggulu in the quantity of 12%. Gokshura [Tribulus terrestris] is the prime ingredient in this being of cold potency, and anabolising effect (madhur vipaka), having nourishing effect strengthening effect, antilithic, anti-diabetic actions and its action is particularly seen on the urinary system. Another important ingredient in this kalpa is musta (Cyperus rotundus). This drug also known by Sanskrit names viz. toyad, ambuvaha, abhra, toyadhar, indicating dominance of water element. In panchabhautik treatment 5 elements are considered viz. pruthvi, jala, teja, vayu, akash. Gokshura is dominant in jala mahabhuta [water element] and hence it is cold in potency whereas guggulu is hot in potency. This unique combination makes it function in the urinary system which is located in the prime site of vata dosha.

2.2. Kanchanar guggulu\textsuperscript{17}

The quantity of guggulu in this formulation is 50% and lekhana action of guggulu is expected from this formulation. Mature [puran] guggulu should be used to manufacture this formulation to achieve kapha alleviating action. Drugs viz. kanchanar (Bauhinia variegata), varuna (crataeva nurvula) are penetrative (bhedaniya), kapha alleviating (kaphaghna), with scraping action on enlarged nodes and glands in neck. Guggulu is excellent drug for lekhana action when it is mature. Hence it assists the other ingredients in this formulation.

2.3. Abha guggulu\textsuperscript{19,24}

Quantity of guggulu is 50% and rest of it is of other ingredients like gum of Acacia arabica [abha], triphala and trikatu combined together. Gum of abha possesses cold potency, unctuous property, nourishing action and leads to union of fracture. Guggulu is also capable of fracture healing and is used with gum of Acacia arabica. Here use of fresh guggulu should be done for better efficacy when one intends to use this formulation for fracture healing, as it is nourishing for tissues. Mature guggulu may be used when we intend to use this formulation for treating osteoarthritis.

2.4. Kaishor guggulu\textsuperscript{9}

This formulation is indicated in gout (vatarakta), skin diseases (kushtha), wounds (vrana), anemia (pandu), diseases of the eye (netra roga) and specifically diseases caused due to blood vitiation (rakta dushti). The quantity of guggulu in this kalpa is 18.13%. Other ingredients include triphala (Terminalia chebula, Terminalia bellerica, Emblica officinalis), amruta (Tinospora cordifolia), trikatu (Zinziber officinale, Piper longum, Piper nigrum), vidang (Embelia ribes), danti (Croton polyandrum), trivrut (Orcypina turpethum) etc. The formulation is indicated in vatarakta , a disease similar to gout ; where the vata and rakta are aggravated. In people of pitta prakruti, performing long hours sitting jobs, aggravation of vata and rakta takes place thus disturbing the natural flow of blood leading to vatarakta. The guggulu in the kaishor guggulu with its unique properties clears off the obstruction in the path of rakta and vata alleviation takes place. Guggulu due to its hot potency may lead to further rakta vitiation; therefore, to prevent this such small quantity (18%) of guggulu must have been included here.

2.5. Chandraprabha vati\textsuperscript{10}

Guggulu and shilajatu are primary and main drugs respectively in this formulation and have been used in maximum quantity compared with the other dravya in the formulation. The vati has been indicated in many diseases. For instance the dravyas like vacha (Acorus calamus), musta (Cyperus rotundus) kiratatikta (Swertia chirata), haridra(Curcuma longa), ativisha(Aconitum heterophyllum), darvi(Berberis aristata), pippali(Piper longum) etc belong to lekhania drug group of Charakasamhita. The formulation must have been prepared using mature guggulu for catabolic action to treat calculi. Similarly, when aphrodisiac action (vrisya karma) is expected the form should be prepared with fresh guggulu.\textsuperscript{33}

3. Significance of percentage of guggulu in its formulations in view of pharmaceutics -

Guggulu formulations are manufactured by following methods.

1. Somapaka (preparations by intense pounding only, no heat is applied.
2. Agnipaka (preparations using heat.
3. Aditya paka (preparations using sunlight.

When we consider the option of compression at industry level manufacturing, the quantity of excipients would depend upon the percentage of guggulu in the formulation. Guggulu itself is a gum resin and hence additional binders may not be required. The combination of excipients is important as there is always a challenge of exceeding the normal limits of disintegration time in case of guggulu tablets. Disintegrators and lubricants need to be used in proper proportions.

It has been reported in a study conducted for triphala guggulu vati, four types of samples were prepared by direct compression, somapaka (pounding), agnipaka (by heat) and aditya paka (by sunlight). This formulation contains guggulu in 55.55% hence no additional binder was required. The powder of triphala guggulu was directly compressed to get good quality tablets. Excipients like binder, glidant, lubricant, and anti-adherent were not used.

4. A General note on excipients

Excipients are the additives used to convert pharmacologically active compounds into pharmaceutical tablets suitable for administration to patients.

International pharmaceutical excipients council (IPEC) defined excipients as the other substances in pharmaceutical formulation other than the active pharmaceutical ingredients which have been appropriately evaluated for the safety in order to help in processing, manufacturing, protection and give support or to enhance stability or to assist in product identification [by use of colourants] or improve any features of safety or effectiveness of drug delivery system during storage or use.35

Excipients for tableting includes following different substances.

4.1. Diluents

The substances acting as a bulking agent or filling material like sugars, lactose, mannitol etc.

4.2. Binders and adhesives

These substances hold powders together to form granules for tableting for e.g. natural gums like guar gum, gum acacia, guggulu, sugars, glucose, syrup polymers, starch, gelatine or synthetic celluloses.

4.3. Glidants

These substances improve the flow of granules from the hopper to the die cavity of tabletting machine to ensure uniform fill for each tablet for e.g. fine silica, magnesium stearate, purified talc.

4.4. Disintegrants

These substances facilitate the breakup of a tablet in the gastrointestinal tract for e.g. starch and derivatives (polyplosdone XL) microcrystalline cellulose clays, algins, gums, surfactants.

4.5. Lubricants

These substances reduce the friction between the granules and the die wall during compression and ejection of the tableting process for e.g. metal stearates, stearic acid, talc (Water-insoluble), boric acid, sodium chloride, benzoate and acetate, sodium or magnesium lauryl sulphate (water-soluble).

4.6. Anti-adherents

These substances minimize the problem of picking, i.e. portion of the tablet face picked out and adhered to the punch face during tableting for e.g. talc, corn starch, metal stearates, sodium lauryl sulphate.

5. Guggulu as a binder for allopathic drug

It’s interesting to know that gum from guggulu was extracted and used as a binder for paracetamol tablet in 4 different concentrations [2%, 4%, 6%, 8%] and gum guggulu exhibited good binding property in uncoated tablets with 90% of drug release in 70 mins of dissolution.[40] However, such use of guggulu as a binder in allopathy is rare. Considering its action against diabetes and arthritis, it may be used as an effective binder synergistically assisting the action of other drugs.

In the recent times there have been important developments in the field of pharmaceutics regarding different dosage forms for the ones existing as well as new designed drugs, synthetic, semi synthetic and natural excipients need to be used for different purposes. Synthetic excipients might cause harm to the body and that’s the reason researchers are interested and looking for excipients from natural resources. Excipients from natural resources possess own properties which can enhance the efficacy of the drug. The natural excipients have an edge over synthetic excipients for, the natural excipients are biodegradable, non-toxic, low cost, environment friendly, having abundant availability, acceptance-palatability.

For guggulu formulations these excipients can be used as follows- Traditionally the guggulu formulations are made by rolling the pills by hands or by pill making machine. It would be appropriate to add some modern disintegrants while formulating guggulu formulations by compression method so that we can reduce the disintegration time; which is reported to be above 1 hour for traditionally made guggulu pills.35 As a lubricant the Ayurvedic physicians use ghee to prevent adhesion to hands.36 The challenges in traditionally
prepared guggulu pills are related to its quality control. More research is needed in this area.

6. Conclusion
Guggulu formulations of Ayurveda are unique, as Guggulu is a natural binder as well as an excellent medicine itself. There are many challenges in manufacturing high quality Guggulu formulations. Hence the formulations were reviewed for their constitutions so that addition of proper disintegrants, and skipping additional binders can be employed while small- and large-scale production of Guggulu formulations. The percentage of this gum resin has been reviewed for assisting the drug research in this field.

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8. Conflicts of Interest
All contributing authors declare no conflicts of interest.

9. Source of Funding
None.

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