

Myrrh a traditional medicine or a multipurpose pharmaceutical excipient

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Abstract

A drug dosage form contains excipients as well as active pharmaceutical ingredients. Formerly, excipients were considered inert components that were used by a formulator to provide the suitable volume, weight and consistency of a dosage form. Today, however, excipients are expected to perform multifunctional roles such as enhancing physical, chemical and microbial stabilities of the dosage form, improving the color or odor of the formulation, and influencing the release and bioavailability of the active ingredient. Among various excipients, natural ones seem to be more beneficial to use, since they are economical, safe, biodegradable, and biocompatible. In this article, myrrh oleo-gum-resin is introduced as a potential natural multipurpose excipient that can perform many useful roles in pharmaceutical dosage forms. Scopus and Google scholar electronic databases were searched to find different properties of myrrh as an excipient. Moreover, ten famous traditional Iranian medicine books were studied to find semisolid formulations named Sabgh, which contained myrrh. One of these formulations was prepared, and its physical and microbiological stabilities were assessed. The role of myrrh as an excipient in this formulation is discussed here. Antibacterial and preservative effects shown in the formulation were related to the essential oil of myrrh. The gum portion was found to be a potential surfactant. In addition, myrrh is a natural muco-adhesive and film forming material. These properties were observed for myrrh in the Sabgh formulation in this study as well. So we can conclude that myrrh could be a potential multipurpose excipient in pharmaceutical industries, which needs further research.

Keywords: Burseraceae, Excipient, Film forming agent, Preservative, Surfactant.

1. Introduction

A drug dosage form usually contains an active pharmaceutical ingredient (API) and a few excipients. Formerly, excipients were considered inactive ingredients in a drug product that would assist manufacturing the dosage form. They were supposed to act as lubricant, filler, disintegrant, emulsifier, suspending agent, and etc. (1). More-

over, by upgrading organoleptic properties of a formulation, they could make it more acceptable for the patients (2). Today, excipients are considered as necessary parts of a formulation that are added to accomplish specific and important roles (3). In novel drug delivery systems, excipients are supposed to enhance the rate of drug release and absorption. It is likely that an API in a formulation has a different bioavailability from the same API in another formulation with the same dosage form due to their different applied excipients (4).

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Recently herbal materials are replacing synthetic pharmaceutical excipients (1). Patients now are more interested in natural drug and cosmetics. Natural excipients are more economic and less toxic than synthetic ones. Furthermore, their biodegradability makes them suitable for application in drug delivery systems. Volatile oils and polysaccharides, such as pectins, alginates, starches and gums are examples of widely used natural excipients. Polysaccharides, which are natural polymers of monosaccharides, are able to play many different roles in pharmaceutical products. They can be used as excipients and act as disintegrant, binder, film former, release modifier, viscosity enhancer, stabilizer, mucoadhesive agent, emulsifier and suspending agent.

In addition, as polymers, they have unique properties that cannot be attained by using other common excipients (5). Today, polymers like oleo-gum-resins of frankincense and myrrh are used widely in food, pharmaceutical and cosmetic industries. These compounds play an important role in the economy of African countries (6). Somalia, Ethiopia and Kenya are now the largest producers and exporters of oleo-gum-resins (7).

Traditional medicines of the world are sources of natural formulations. They contain thousands of formulations that have been formulated as dosage forms by ancient formulators (8). Today, pharmaceutical industries and academic researchers show more interest in the researches performed on these formulations (9). But the search is usually done to find new active compounds to cure or manage clinical diseases (10). Traditional formulations, however, have the potential of being studied pharmaceutically as well. They are multicomponent formulations that contain not only active ingredients, but also excipients. So these formulations are good sources to find potential natural pharmaceutical excipients. One of the traditional systems of medicine, which is still being practiced, is traditional Iranian medicine (TIM). There are many books and written sources available today that contain thousands of Iranian pharmaceutical formulations. Studying these formulations gives us the opportunity to find naturally derived excipients. One of the materials that has been used in the formulations of TIM

is the gum derived from *Commiphora myrrha*.

Commiphora myrrha (syn: *C.molmol*) from the family of Burseraceae, is an endemic plant of northeast Africa (11) and Arabia (12). The shrubs of *Commiphora myrrha* secrete a natural reddish-brown oleo-gum-resin named myrrh (13). The term myrrh is derived from the Arabic and Hebrew word Murr, which means bitter (14).

Myrrh has a rich history of use in the world. There are more than 800 herbal medical compounds in Ebers Papyrus, most of which contain myrrh and honey (15). It is believed that myrrh was one of the three gifts given to the Christ child by Magi (14). The ancient Egyptians used myrrh for embalming (11). It was used to treat diseases like arthritis, parasitic infections, gastrointestinal diseases and also for treatment of wounds, fractures and pain (16) in traditional medicine of China, India, Greece, Roma, Babylon (17) and Iran. In Iranian traditional treatises, myrrh was used for its antibacterial properties on wounds, ear, eye, mouth, and gynecological infections (18). Other than the formulations that were designed to treat infections, myrrh has been used in semisolid cosmeceutical dosage forms as well (19). One of these dosage forms are Sabigh (singular: Sabgh) in TIM. These formulations were designed to cover skin flaws such as pigmentation problems and scars (18).

Myrrh contains a water soluble gum portion and an oleo-resin part, which is soluble in alcohol (11). Terpenoids, steroids, flavonoids, lignans, carbohydrates, and long chain aliphatic alcohol derivatives have been isolated from different species of *Commiphora* (20). Myrrh contains 23- 40% resin, 40- 60% gum and 2-8% essential oil. The resin part of myrrh contains α , β , and γ -commiphoric acid, commiphoric acid, heeraboresene, α and β -heerabomyrrhols, commiferin, kosteroids, campesterol, β -sitosterol, cholesterol, α -amyrone and 3-epi- α -amyrin (21). The gum consists of 18% protein and 64% carbohydrate. The carbohydrate portion of the gum has a similar chemical structure to acacia gum (14). Hydrolysis of the gum results in arabinose, galactose, xylose, and 4-O-mythylglucuronic acid (21). Its viscous essential oil has pale yellow color (14) and contains about 20 different furanosesquiterpenoids (22), which are responsible for characteristic odor of myrrh (23).

The presence of three components that makes myrrh an oleo-gum-resin and also its application in semisolid formulations of TIM, make us believe that it might have the potential of acting as a multipurpose excipient in pharmaceutical dosage forms.

2. Materials and methods

The possible potentials of myrrh gum which could make it a suitable pharmaceutical excipient were searched in the Google scholar and Scopus data bases. The last search was performed in August of 2015. Three major parts of myrrh, which are essential oil, resin and gum were searched separately. The key words included *Commiphora myrrha*, antimicrobial preservative, natural excipient, surfactant, and bio-adhesive. In the next step, we searched 10 of the TIM books for a semisolid formulation, where myrrh could show its properties as a pharmaceutical excipient. Sabigh were found to be a suitable choice for further research. They are semisolid formulations that were used to cover skin problems in TIM. Myrrh is one of the most frequent ingredients in Sabigh. We studied Sabigh formulations and identified their ingredients. We then listed Sabigh, which contained myrrh and prepared one of them to study the role of myrrh in the semisolid formulations. The prepared Sabgh was kept in 25 °C for one year to study its physical and microbiological stabilities. The physical stability was evaluated by visual analysis and detection of any phase separation.

Microbiological examination was carried out with 1g of the formulation sample. One gram of the formulation was diluted in the validated nourishing diluents and a 1 in 10 dilution was obtained. Casein-peptone lecithin polysorbate broth (base) was the diluent for the total count of bacteria and also for the enumeration of yeast and mold. The microbial stability was studied on the basis of total count of microorganisms. The prepared diluted sample (1 ml) was added to 10 cm diameter petri dishes. The temperature of about 15 ml of molten Tryptic soy agar medium was not more than 45 °C. Each petri dish was mixed and maintained on a cool horizontal surface until solidified. Plates were incubated at 30 to 35 °C for bacteria and other plates at 20 to 21 °C for fungi. The num-

ber of colonies developed was counted after 3 days for bacteria and 5 days for fungi. This process was repeated after one year for the Sabgh kept at 25 °C.

3. Results

Myrrh was found as an oleo-gum-resin with a broad range of useful properties as a potential pharmaceutical excipient in electronic databases. It possesses antimicrobial and antifungal characteristics (14) that have been attributed to its essential oil (24). Application of myrrh due to its antibacterial properties is referred to Sumerians in 1100 BC, who used myrrh to treat infected teeth. Moreover, it has been used for treatment of skin candidiasis (25). Myrrh was also an essential component in Egyptian mummification. Egyptians filled dead bodies with crushed myrrh. It was used as an antiseptic in mummification. Furthermore, myrrh odor made the mummy fragrant (26). Also, new studies have proved myrrh antibacterial and antifungal effects against *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Candida albicans* (27).

There are studies that introduced the whole gum as a tablet binder and drug release retardant. Moreover, its potentials as a natural muco-adhesive agent have been investigated (13).

The crude gum portion of myrrh consists of about 70% 4-methyl-glucuronogalactone protein. After extraction with 90 % alcohol and clearing the resin away, polysaccharides are left. D-galactose, L-arabinose and 4-methyl D-glucuronic acid were detected in this fragment (28).

Myrrh is also a safe ingredient as a flavoring agent in food industry and has been given GRAS status (generally regarded as safe) (14).

After studying traditional Iranian treatises, thirty eight Sabgh formulations were found. The frequency of application of myrrh as an ingredient in these formulations was determined 31.58%. The formulations that contain myrrh are shown in table 1.

A Sabgh, consisting of myrrh, was formulated according to traditional Iranian books. The ingredients were: *Commiphora myrrha* (Nees) Engl., *Rubiua tinctorum* L. (Rubiaceae), alum, saltpeter, Armenian bole, khabasol-hadid (Iron oxide), vinegar and ethanol. (Khabas-ol-hadid is the pieces of metal that

Table 1. Ingredients of the Sabigh formulations which contain myrrh.

No.	Ingredients
1	<i>Commiphora myrrha</i> , <i>Anacyclus pyrethrum</i> , <i>Lycium afrum</i> , <i>Brassica nigra</i> , <i>Nigella sativa</i> , <i>Anemone sp.</i> , <i>Rubiua tinctorum</i> , <i>Lepidium latifolium</i> , orpiment, goat blood
2	<i>Commiphora myrrha</i> , <i>Indigofera tinctoria</i> , <i>Rubiua tinctorum</i> , khabas- ol-hadid, wine debris
3	<i>Commiphora myrrha</i> , <i>Rubiua tinctorum</i> , <i>Lepidium latifolium</i> , <i>Indigofera tinctoria</i> , <i>Isatis tinctoria</i> , alum, saltpeter, khabas- ol- hadid, Armenian bole, wine debris, vinegar
4	<i>Commiphora myrrha</i> , <i>Loranthus europaeus</i> , <i>Rubiua tinctorum</i> , Armenian bole, alum, borax, wine debris
5	<i>Commiphora myrrha</i> , <i>Rubiua tinctorum</i> , alum, saltpeter, wine debris
6	<i>Commiphora myrrha</i> , <i>Rubiua tinctorum</i> , alum, wine debris
7	<i>Commiphora myrrha</i> , <i>Lepidium latifolium</i> , <i>Helleborus niger</i> , <i>Nigella sativa</i> , <i>Brassica nigra</i> , <i>Lycium afrum</i> , <i>Anemone sp.</i> , <i>Quercus lusitanica</i> , <i>Senegalia senegal</i> , orpiment, alum, vinegar
8	<i>Commiphora myrrha</i> , <i>Anacyclus pyrethrum</i> , <i>Lepidium latifolium</i> , <i>Anemone sp.</i> , <i>Rubiua tinctorum</i> , <i>Lycium afrum</i> , <i>Brassica nigra</i> , <i>Nigella sativa</i> , <i>Curcuma longa</i> , orpiment, goat blood
9	<i>Commiphora myrrha</i> , <i>Punica granatum</i> , khabas- ol- hadid
10	<i>Commiphora myrrha</i> , <i>Rubiua tinctorum</i> , <i>Lepidium latifolium</i> , <i>Indigofera tinctoria</i> , <i>Isatis tinctoria</i> , Armenian bole, khabas- ol- hadid, alum, saltpeter, vinegar, wine debris
11	<i>Commiphora myrrha</i> , <i>Quercus lusitanica</i> , Cuttlefish bone, Asphaltum
12	<i>Commiphora myrrha</i> , <i>Rubiua tinctorum</i> , Armenian bole, alum, saltpeter, wine debris, vinegar

are separated from iron during the process of forging (29). According to the text books of TIM, these iron pieces should be processed before use in the formulations. After that, the powder is called Khabas-ol-hadid (30)).

Physical stability of the prepared Sabgh was determined by visual analysis. It was physically stable after one year; as despite of having solid particles and oil portion in the formulation, it stayed homogeneous in a one year period, and no phase separation was observed. This stability may be attributed to the presence of myrrh. Since the gum portion of myrrh is similar to acacia gum (the most widely used herbal emulsifier) (14), it can be considered as a surfactant, which provides physical stability. Acacia contains a highly branched compact arabinogalactan with a central protein that makes the gum a suitable emulsifying agent (31).

The Sabgh was also microbiologically stable after one year. The number of bacteria per gram was less than 100 colonies at the preparation time which is less than the acceptable limit for topical products according to USP 2012 (200 colonies per gram) (32). There were also no yeast and mold growth on the test plates. After one year, the total count of microorganisms showed no microbial growth. Microbiological stability may be related to myrrh essential oil, whose antibac-

terial and antifungal properties has been proved.

The formulation formed a film on the skin, which is probably due to presence of the resin part of myrrh. The film forming property was not seen after extraction of myrrh with alcohol and removing the resin fragment.

4. Discussion

Myrrh oleo-gum-resin is a useful ingredient in pharmaceutical dosage forms. Its antibacterial properties were well known since ancient times. It has been shown in a study that terpenes from the oleo-resin of myrrh have antibacterial effects against some strains of *Staphylococcus aureus*. Abdallah *et al.* (33) used petroleum ether, ethyl acetate, methanol and de-ionized distilled water to prepare the extract of myrrh. The methanolic extract which contains the essential oils showed the most antibacterial effect. In addition, myrrh essential oil has potential anti-fungal effects. Its MIC against *Aspergillus flavus* was determined 3.0 µl/ml in a study, while synthetic preservatives like BHT, ascorbic acid and gallic acid had an MIC up to 10 µl/ml. Also the MIC of myrrh against nine food borne molds including *Aspergillus niger* was 2.5 to 3.5 µl/ml (34). The essential oil of myrrh showed no inhibitory effect against *Pseudomonas* in a study done by Wanner *et al.*

(35); but Dolara *et al.* (27) showed that sesquiterpenes of myrrh possess antibacterial and antifungal effects against standard pathogenic strains of *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Candida albicans* with MIC equal to 0.18 to 2.8 µg/ml. As a result, microbiological stability of the formulated Sabgh in one year can be related to myrrh essential oil.

The chemical structure of water soluble portion of myrrh which is similar to acacia gum (14) could make us consider this gum as a potential surfactant. The Sabgh formulated in this study was physically stable after one year and no phase separation occurred. We can consider the gum portion of myrrh as a surfactant in this formulation, but since there are not enough studies in this area, this can only be discussed as a theory.

Myrrh was introduced as a muco-adhesive agent in a study done by Arora *et al.* (13). The formulated Sabgh had bioadhesive properties as well and formed a film on the skin. These properties could be attributed to the resin portion of myrrh, however further studies are needed to confirm this theory.

Myrrh acted as a surfactant, preservative and a film forming agent in the Sabgh for-

mulated in this study. As a result, we can introduce myrrh as a potential multipurpose excipient.

5. Conclusion

Myrrh oleo-gum-resin is a natural compound, which was widely used in TIM and mostly in semisolid formulations. New studies have found many properties for myrrh in pharmaceutical dosage forms. It has proven emulsifying, mucoadhesive, tablet binder, drug release retardant and antibacterial properties. So, it can be considered as a potential natural multipurpose excipient in pharmaceutical formulations. Further researches are needed to confirm myrrh oleo-gum-resin as a pharmaceutical excipient.

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Conflict of Interest

None declared.

6. References

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