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A Review

Future prospects of fermentation in unani based drugs

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Unani system of medicine is being practiced in India for hundreds of years for treating various ailments by its holistic approach with natural means and drugs. Unani formulations are based on herbal, mineral and animal origin. Till date, there is no major development in different forms of the drugs and are being used as they are mentioned in the classical literature. There is need of the hour to devise pharmaceutical processing techniques to achieve palatability, more stability, absorption and assimilability of both single and compound Unani drugs without deviating from the original essence as described in the literature. Fermentation (*Takhmīr*) may be explored as a unique tool for the modification of dosage forms for herbal Unani drugs. It is a process of chemical change caused by organisms or their products for transformation to another compound of medicinal value. It extracts a wide range of active ingredients from the herb than any other methods of extraction. During fermentation, undesirable molecules like sugars are removed from plant extracts and made the product more bio-available and stable, less toxic and more efficient. In the Unani system of medicine, various products have been mentioned in classical literature where the process of the fermentation is applied for the preparation of drugs like *Sirka, Nabeez, Dar Bahra, etc*. Fermentation based drugs used in Ayurveda are Asvas and Arishthas are generally found superior to extracts for absorption in the gut with enhanced therapeutic properties, quicker action, and longer shelf life. In order to achieve better therapeutics in Unani Drugs, the process of development of compound formulation based on fermentation should be adopted for different forms of Unani formulations.

Keywords: Bioavailability, Fermentation, *Jawarishat*, *Majoonat*, Pharmaceutical, Therapeutic

Introduction

The Unani system of medicine is one of the traditional health care systems practiced in India for the last hundreds of years. It has been developed through the beliefs, experiences, and theories indigenous in nature. The intended use of Unani drugs for diagnosis, treatment, mitigation or prevention of diseases is clearly defined in the Drugs and Cosmetic act 1940[1]. The majority of drugs used in the Unani system of medicine are comprised of around 400-700 medicinal herbs[2]. These herbal drugs are generally considered as cheaper and safe. About 80% of the world's population uses herbal medicines as part of their primary health care needs[3]. Herbs and plants can be processed and used in different ways and forms. The general method for herbal drug preparation includes three phases[4] as given in (Table 1).

The extraction process is the most important step in the preparation of the herbal drug. During this step, bioactive and nutritive molecules present in the herbs are released into the medium. There are many other modern extraction techniques available like mashing, maceration, solid-phase extraction, fermentation, *etc*. Among these techniques, fermentation is gaining interest in the scientific community to produce novel active compounds with potent medicinal values during herbal drug preparation. The current review summarizes the advantages and significance of using fermentation technique for the preparation of herbal drug and its future application in Unani system of medicine.

Fermentation

Fermentation is a process of chemical change caused by microorganism for transformation to another compoun d of medicinal value . During fermentation, the plant cells rupture more efficiently and hence a wider range of active ingredients are exposed to the menstruum. The alcohol produced during the fermentation process help in releasing the compounds from the cells to the medium[5,6]. The microorganism used in the fermentation releases various types of enzymes which disintegrate the herbal medicines or the target molecules and convert them into new entities of medicinal value[7]. In

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Table 1 — Phases in the general method for herbal drug preparation

Phase	Name of the Phase	Activities
I	Pre-processing	Washing, Drying And Cleaning Activities of Herbs
II	Extraction Process	The bioactive compounds are released from the medicinal plant
II	Separation Process	Desirable Compounds are Separated From the Unwanted Plant Components

addition, microorganism uses active herbal ingredients as substrates or secondary metabolites produced during fermentation interact with each other to produce new compounds or modify the naturally occurring molecules such as isoflavones, saponins, phytosterols, and phenols and thus exert more therapeutic potencies and lowers the toxicity. The non-medicinal components, such as proteins, sugars, and other substances are also removed during fermentation making the herbal drugs more bio-available and safe[8,9].

Biochemical changes during fermentation

Several biochemical changes occurred during the fermentation process which results in the alteration of nutritive and anti-nutritive components of the plants making the plant product more therapeutic and safe. Previous studies showed that fermented herbs have anti-oxidative[10], anti-diarrheal[11], anti-inflammatory[12], anti-obesity[13] and anti-diabetic properties[14] making the fermented herbal drugs more bioactive, stable and longer shelf life[9,15,16]. Fermentation transforms the phytochemical compounds of the medicinal plants and thus rendering them with a sweet taste, less toxic, more potent and more absorption[17-19]. In a study, an investigation was carried out to find the differences between the components of LM-Arishta (fermented Herbal liquor) prepared from ginger, jujube and long pepper, and a tincture derived from the same ingredients (alcohol-soaked herbal liquor) and it was found that the concentration of metabolite gingerol in LM-Arishta was less than 50% of that of the tincture due to the transformation of [6]-gingerol to metabolites such as [6]-shogaol and 3 or 5 acetoxy-[6]-gingerdiol during alcoholic fermentation[17]. In another study, the inhibition of PLA_2 by the berberine and biotransformed berberine generated by alcoholic fermentation was assessed and it was found that the hydroxyl derivatives of berberine produced during fermentation produced had a higher inhibitory towards phospholipase A2 (PLA_2)[20,21]. Study conducted on fermented Oyaksungisan, a traditional medication in Asian countries showed that the fermented extract strongly inhibited the production of pro-inflammatory mediators including NO, PGE_2, TNF-α and IL-6 and their synthesis enzymes iNOS and COX-2[22]. Another study conducted on Radix astragali (RA), a traditional Chinese medicinal herb, fermented using Aspergillus spp, showed that the fermented RA exerted much stronger anti-oxidant activities by increasing the phenolic compounds than those of unfermented RA[23]. In Korea and China Ginseng has long been traditionally used to treat various diseases. The metabolite content of wild ginseng (WG) and Fermented Wild Ginseng (FWG) was determined using HPLC and it was found that the contents of C-K, 20(S)-protopanaxatriol (PPT), Rh1, F1 and 20(S)-protopanaxadiol (PPD) increased drastically in FWG. The overall results showed that FWG contains more active ginsenosides than non-fermented wild ginseng, suggesting that FWG may have more bioavailable, bioactive and therapeutic effects[24]. There are lots of other studies which showed that biochemical changes have been found during the fermentation process of extracts of the herbs.

Fermentation in the unani system of medicine

Takhmīr is the chemical conversion of sugars into ethanol. It's possible English equivalent is fermentation. In the Unani system of medicine, various products have been mentioned in classical literature where the process of fermentation is applied for the preparation of drugs like *Sirka*, *Nabeez*, *Dar Bahra*, *Aabkaama*, *etc*. The preparation of sirka is well described in the Unani system of medicine. A microorganism called *Ummul khal* (mother of vinegar) or mycoderma aceti play a key role in the process of fermentation[25]. However, in ancient time, the involvement of a microorganism in the process of fermentation may be unknown. *Sirka* possesses anti-infective, anti-hypertensive, cardio-protective, anti-tumor, anti-oxidant activities[26]. *Aabkaama, Muri, and Kanji* are also a liquid preparation made up of *Rae, Namak* and *Ajwain* with the same procedure as *Sirka*. *Sikanjabīn* is also prescribed in Unani literatures made with vinegar and honey but later honey was substituted with sugar. It is of many types like *Sikanjabīn Asuli* (roots), *Sikanjabīn Bazuri* (seeds), *Sikanjabīn lemuni* (Lemon), *Sikanjabīn unsuli* (Piyaz) and *Sikanjabīn fawakiha* (Friuts), *etc*[27-31]. *Nabeez* is a dosage form used in the earlier era of Unani medicine obtained by the fermentation of sweet aqueous solutions of various food grains, fruits and

Table 2 — Dosage forms in Unani system of medicine

S. No	Dosage form	Examples
1	Solid dosage form	Pills, tablet, powder, *etc*.
2	Semi-Solid dosage form	Majoon, Jawarish, Itrifal, *etc*.
3	Liquid dosage form	Sharbat, Shikanjabeen, Arq, *etc*.
4	Gaseous dosage form	Bakhoor, Shamoom, *etc*.

medicinal ingredients for a specific period of time. There are many types of *Nabeez* formulations mentioned in Unani literature mostly named against their chief constituent[32]. It is prepared by keeping the decoction of the herbal drug in the form of a solution of sugar or jaggery in a container whereas in *Dar Bahra*, the cold infusion of the drugs is used to make the solution with Sugar, Jaggery, Honey, *etc*. The fear of intoxication in manufacturing methodology makes *Nabeez* and other fermented Unani formulations unpopular in India. The previous study showed that the modification in the manufacturing procedures of *Nabeez* is beneficial for the improvement of quality of the product and economy[32].

Perspective dosage forms

The administration of drugs obtained from plant, animal and mineral source in their crude forms are generally not recommended due to issues like product quality, inaccurate measurement of dose, *etc*. To overcome this problem, the drugs are formulated into dosage forms so that products quality, accurate dosage, the convenience of administration, *etc*. persist[33,34]. In the Unani system of medicine, the dosage forms can be classified into four types as given in (Table 2).

Till date, the Unani dosage forms or formulations are maintained as like they were discovered. At present more than 60 dosage forms of Unani drugs are reported in different Unani pharmacopoeias but among them, only 20 (33.33 %) dosage forms are popular (Fig. 1). Rest of the 40 (66.66 %) Unani dosage forms are not popular may be due to time-consuming preparations, difficult to carry, the large bulk of dosage, unsterilized method of handling, delayed action, high sugar content, *etc*[33,35]. However, some modifications have been made which are not sufficient[35]. The formulation should be lucrative, palatable, age-appropriate dosage form and patient's centric[36].

Conventional dosage forms are not suitable in certain conditions due to many reasons *e.g.* Solid dosage form may not be suitable for patient with swallowing difficulties. The disadvantages with

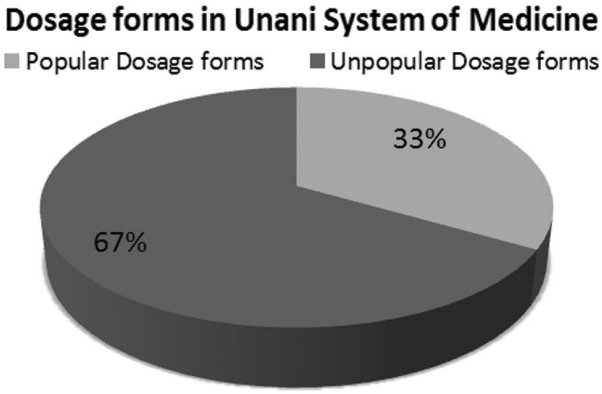

Fig.1 — Distribution of dosage forms according to usage

semi-solid dosage forms such as *Majoonat* and *Jawarishat* is that these are bulky, having a higher percentage of sugar, undergo chemical gas formation and inaccurate drug measurement, *etc*. The growing demand of herbal drugs made it also necessary to provide adequate stability for long-term storage and safety of the herbal drug. As the herbal formulation is a mixture of more than one active ingredient, it is often prone to deterioration, especially during storage, leading to loss of active component. Besides providing palatable, age-appropriate and patient's centric dosage forms, stability, *etc.*, the dosage forms are also required to provide optimal drug action, Protection from gastric juice, sustained and controlled release of medication, placement of drug directly inside the bloodstream and to protect the drug substance from the destructive influences of atmospheric oxygen or humidity[33]. Modifications of the conventional herbal formulations can deal with the above-mentioned problems to a large extent[37]. The preparation of Unani formulation should be made in such form, which may be used in minimum dose with high efficacy and safety.

The Fermented dosage form in other systems of medicine

In contrast to Unani Medicine, Ayurvedic and other systems of medicines have changed drug dosage forms according to the need of the time. Biomedical fermented formulations are considered as one of the best dosage forms of Ayurveda in practice for thousands of years. Fermented products have now demonstrated its ascendancy on other dosage forms of Ayurveda[20]. Asavas and Arishthas are the fermentation- based drugs used in Ayurveda which are prepared with the natural fermentation process, are generally found superior to extracts for absorption in the gut with enhanced therapeutic properties, quicker action and longer shelf life[38]. Arishtas are

prepared in the airtight sealed vessel by anaerobic fermentation of decoction of plant material, sugar and dried flowers of *Woodfordia fruticosa* (L.) Kurz (Lythraceae). The Arjunarishta, the fermented product is palatable to use because of sweet taste combined with a fine aroma. The alcohol generated during the process act as a preservative and improves stability of formulation[17]. Another fermented Ayurvedic product is Kanji which is found nourishing, relive burning sensation, relive thursts, *etc*. It is also used for purification of metals[39]. Also, the studies conducted in past years on ginseng, a chinese medicinal herb, showed that the fermented ginseng is more potent, stable, bioavailable and therapeutic than non-fermented ginseng[40]. Nowadays, fermentation is gaining popularity to produce novel active compounds with potent medicinal values during herbal drug preparation and hence the process of development of compound formulation based on fermentation should be adopted for different forms of Unani formulations.

Conclusion

The formulations generally used in Unani system of medicine are Qurs, Habb, Shiyaf, Sufoof, Rub, Majoon, Itrifal, Jawarish, Gulqand, Maul Jubn, Mau Shaeer, Sharbat, Joshanda, Haleeb, Zulal, Inkabab, Shumoom, *etc*. Fermentation in Unani system of medicine is generally not considered for development as novel formulations owing to lack of scientific justification and processing difficulties. Now it is high time to standardize the process on modern parameters. Considering the significance of biomedical fermentation in other systems of medicine, exploration of new dosage forms and also need of revival of *Nabeez* and *Dar Bahra* in Unani system of medicine is required. Process of fermentation may be applied in some of these formulations to increase their absorption and action with the added benefit of better preservation due to alcoholic content. Every possibility for the advancement and acceptability of these fermented dosage forms in the Unani system of medicine from the perspectives of pharmaceutical progress, bioavailability, therapeutic, safety and commercial issues must be explored broadly.

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