Research Article

Development of New dosage form of Majoon Aarad Khurma- A Unani formulation for sexually weak Diabetic patients

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ABSTRACT

Air, water, food and reproduction are four basic things which are essential for the propagation of human race, and for reproduction, sexual act is necessary. Sexual function is an important component of quality of life and subjective well being of humans. Diabetes results in ED in 50-75% of men. In men with diabetes, the incidence of ED is 9% from age 20 to 29 years; and increases to 95% by age 70. Majoon Aarad Khurma is one of the most important and common drug for aphrodisiac activity in present days and in ancient time. It is an important Pharmacopeial preparation of Unani system of medicine which is commonly used in various sexual diseases and related conditions . In present study an important Unani compound formulation Majoon Aarad Khurma has been modified into granular form using natural sweetening agent *Stevia rebaudiana* which has sweetening property as well as hypoglycemic activity.Thus, keeping in view the above consideration, physico-chemical standardization of the test drug GMAK was evaluated. The granules of Majoon Aarad Khurma were found to be more stable, convenient and comfortable in usage and dispensing, and also safe, light, efficacious, cost effective and quality controlled, palatable and will not cause any harm to diabetic patients who are suffering from sexual dysfunction.

Keywords: Aphrodisiac, Diabetes, Sexual dysfunction, Granules, *Stevia rebaudiana*, CCRUM, Sweetening agent.

INTRODUCTION

The Unani system of medicine offers a number of drugs useful in the management of sexual dysfunction.[1] An aphrodisiac is a drug or an agent which increases sexual arousal and stimulate sexual desire. The name comes from the Greek Goddess of sexuality Aphrodite [2]. The aphrodisiac agents are widely varied in nature.[2] The aphrodisiac have been categorized into Muqawwie Bah, Mughallize Mani, and Muharrike Bah. [3] Sexual dysfunction is of major concern to people with diabetes. A survey of men with diabetes found that they were prepared to pay more for the treatment of their erectile dysfunction than for any other diabetes-related complication, except blindness and renal failure [4-7]. Likelihood of erectile dysfunction increases with age but is not an inevitable consequence of ageing. The onset of erectile dysfunction occurs earlier in the diabetic population; in fact, impotence affects diabetic patients at an average of 10 to 15 years earlier than in the general population [8-14].

Granulation is the process in which primary powder particles are made to adhere to form larger multi particle entities called granules. Granular materials may also be used as dosage forms for oral administration, which can be swallowed as such, chewed, or dispersed in water or suitable liquid before consumption.[15, 16-17] Among men with erectile dysfunction, those with diabetes may experience the problem as much as 10 to 15 years earlier than men without diabetes. Research suggests that erectile dysfunction may be early markers of diabetes, particularly in men aged 45 and younger.

Stevia is a subtropical perennial that produces sweet steviol glycosides in the leaves for which it also known as ‘Cheeni Tulsi’ or ‘Mou Tulsi’. Plants grown at higher latitudes actually have a higher percentage of sweet glycosides. The plant can be utilized as a source for the

production of a natural sweetener (food). Stevia leaves are 20-30 times sweeter than sugar.

Stevioside is one of the important the leaf of Stevia (5-10% of dry weight basis) and is 300-350 times sweeter than sucrose.[18] In the medicinal field, it has hypoglycemic, oral contraceptive, cardiovascular, and antimicrobial activities. It is also used for weight loss, digestive and skin problems[19-21].

The mechanism for the blood glucose-lowering stevioside was elucidated and the impact of stevioside and its aglycon steviol on insulin release from normal mouse islets and the ß-cell line INS-1 were studied. Both stevioside and steviol enhanced insulin secretion from incubated mouse islets in the presence of glucose. Stevioside and steviol had a long-lasting and apparently reversible insulinotropic effect in the presence of glucose and stimulate insulin secretion via a direct action on ß-cells1 [22].

Majoon Aarad Khurma is one such popular drug which is widely used as an effective aphrodisiac, which is prepared with sugar as base but as we know that the intake of sugar is not advisable in diabetic patients because the presence of sugar in large amount in blood may develop the complications of diabetes more rapidly so any preparation having sugar as a base or content may create such risk. So even after gaining such popularity as an aphrodisiac, Majoon Aarad Khurma cannot be given to diabetic patients who are suffering from erectile dysfunction. Hence sugar free an alternate formulation should be innovated or designed to meet the demand of the diabetic patients.

Therefore the present study was aimed to develop granules of Majoon Aarad Khurma with natural sweetening agent *Stevia rebaudiana* in place of sugar, as there are some ingredients in Majoon Aarad Khurma which are rich in carbohydrates and which may increase the level of glucose in blood and as various researches have proved that *Stevie* has hypoglycemic action so it can neutralize the increased glucose level of blood and we can make Granules of Majoon Aarad Khurma a safe remedy for erectile dysfunction in diabetic patients [23].

Physico-chemical standardization are a pre-requisite in quality control of Unani medicines, both single as well as compound. The efficacy of a drug mainly depends upon its physical and chemical properties therefore, the determination of physico-chemical characters for the authenticity of a drug is necessary.

Thus, keeping in view the above consideration, physico-chemical standardization of the test drugs GMAK was carried out. Granules of Majoon Aarad Khurma were prepared and subjected to Physico-Chemical evaluation.

MATERIAL AND METHOD

Formulation of Granules

All the required ingredients of Granules of Majoone Aarad Khurma were procured from the raw drug dealers under the supervision of the Guide, and all the raw drugs were identified and authenticated by the expert Dept. of Ilmul Advia, NIUM Bangalore, (Karnataka). Granules are prepared in the laboratory of Dept. of Ilmul Saidla, NIUM Bangalore, as per the formulation mentioned in the National Formulary of Unani Medicine, Part-1, Govt. of India**.** The composition is as given in table 1: All the dried ingredients were powdered and sieved in (sieve number 80). All the Maghaziyat (kernels) were powdered separately and sieved in (sieve number 40), and dates were separately dried in a hot air oven at 100 °C for 4 hours and then powdered and passed through sieve number 60. *Stevia* plant extract was prepared with 120 ml water at low temperature for 15 minutes, and sieved through muslin cloth; the total quantity of this extract obtained was 80 ml. All the dried drugs were mixed one by one in Stevia extract, and subjected into the granulator (sieve number 20) for formation of granules and then stored in container at room temperature for further study [24].

Table 1: Ingredients of granules of Majoon Aarad Khurma

Sl. No.	UNANI NAME	BOTANICAL NAME	PART USED	QUANTITY
1	Khurma	*Phoenix dactylifera*	Fruit	200gm
2	Kamagh arbi	*Acacia arabica*	Gum	200gm
3	Singhara khushk	*Trapa bispinosa*	Fruit	200gm
4	Satawar	*Asparagus rasemosus*	Root	50gm
5	Jaiphal	*Myristica fragrans*	Nutmeg	1.25gm
6	Javitri	*Myristica fragrans*	Mace	1.25gm
7	Qaranfal	*Myrtus caryophyllus*	Fruit	2.5gm
8	Maghaze Badam	*Prunus amygdalus*	Fruit	25gm
9	Maghaze Chilghoza	*Pinus gerardiana*	Fruit	25gm
10	Maghaze Fundaq	*Corylus avellana*	Fruit	25gm
11	Maghaze Pambadana	*Gossypium herbaceum*	Fruit	5gm
12	Stevia plant powder	*Stevia rebaudeana*	leaves	3.50gm

Physico-Chemical Evaluation

The Physico-Chemical studies were carried out on Granules of Majoon Aarad Khurma in the laboratory of Dept of Ilmul Saidla, NIUM, Bangalore which included organoleptic properties of the granules like appearance, colour, smell, taste, water soluble matter, successive extractive values, pH value, bulk density and tapped density, ash value, Thin layer chromatography (TLC) was also conducted and R_f value were calculated for identification of compounds.

Organoleptic properties [25, 26].

Organoleptic properties of GMAK like appearance, colour, smell and taste were noted

Determination of water soluble matter

Cold maceration method: [27]

Accurately weighed 5.0 g of the samples of GMAK were placed in glass Stoppard conical flask separately. Macerated with 100 ml of the DDW for 6 hours, shaking frequently, and then allowed to stand for 18 hours and filtered rapidly through dry filter paper, and evaporated to dryness on a water-bath. Then dried at 105°C for 6 hours in hot air oven and cooled in desiccators for 30 minutes and weighed instantly. The percentage of water soluble matter was determined.

Successive extractive values [28]

The extractive values of GMAK in different solvents viz. petroleum ether, chloroform, ethyl alcohol and water were carried out by percolation in Soxhlet's apparatus separately and heated for six hours on a water bath for each solvent except water, which was heated directly on a heating mantel. Granules of test samples was taken and subjected to successive extraction with each solvent. The extracts were filtered on water bath; the percentage of extractive values was calculated.

Determination of pH [28,29]

pH of freshly prepared 1% w/w suspension and 10% w/w suspension in 100 ml distilled water of the test samples GMAK was determined using simple glass electrode digital pH meter.

Bulk density & tapped density of granules[29, 30]

30 gm of drug (GMAK) was filled and carefully added them into cylinder with the aid of a funnel without any loss. The cylinder was tapped by a digital tap density apparatus (Lab-India Tap Density Apparatus, Model-TD 1025). The initial volume was noted and the samples were then tapped until no further reduction in volume was noted.

$$\text{Bulk Density} = \frac{Mass}{Bulk\ Volume}$$

$$\text{Tapped Density} = \frac{Mass}{Tapped\ Volume}$$

Carr's Index

$$\text{Carr's Index} = 100\ x\ \frac{1-Db}{Dt}$$

Where D_b = Bulk density, D_t = Tapped density

Hausner Ratio

$$\text{Hausner Ratio} = \frac{Dt}{Db}$$

Where D_b = Bulk density and D_t = Tapped density.

Ash values determination [31, 32]

Total Ash

2 gm of drug GMAK was incinerated in a silica dish at a temperature not exceeding 450°C until free from carbon, cooled and weighed and the percentage of Total Ash was calculated.

Acid insoluble Ash

The ash was boiled with 25ml of dilute hydrochloric acid for 5 minutes. The insoluble matter was collected on an ash less filter paper washed with hot water and ignited at a temperature not exceeding 450°C and weighed after cooling. The percentage of Acid insoluble Ash was calculated.

Water soluble Ash

The ash was boiled with 25 ml of distilled water for 5 minutes. The insoluble matter was collected on an ash less filter paper, washed with hot water and ignited. The weight of insoluble ash was subtracted from the weight of the total ash, giving the weight of the water soluble ash. The percentage of Water soluble Ash was calculated.

Chemical evaluation

Thin layer Chromatography: [33, 34]

Thin layer chromatography was carried out on T.L.C. pre coated aluminium plates, silica gel 60 F 254 (layer thickness 0.25 mm) for ethanolic extract of the test drug samples GMAK in various mobile phases (Toluene: Ethyl acetate (7 : 3, with 2 drop Sulphuric acid), ,. The R_F values of the spots were calculated of the test drug by the following formula.

$$R_f\ \text{Value} = \frac{Distance\ travelled\ by\ Spot}{Distance\ travelled\ by\ Solvent}$$

RESULTS AND DISCUSSION

The organoleptic properties of Granules of Majoon Aarad Khurma was determined on the basis of appearance, color, smell, and taste, was found to be, granular, light brown, pleasant, and sweet.

The **Water soluble matter** of the drug were determined. The percentage of water soluble matter was found to be 36.6 ± 0.50 in Granules of Majoon Aarad Khurma. (shown in table no.2) [35].

The **Extractive value** is a parameter for detecting the adulteration in any drug Therefore, for establishing the standards of any drug these extractive values play an important role, as the adulterated or exhausted drug material will give different values rather than the extractive percentage of the genuine one[111]. Extractive values of the drug were determined. The percentage of extractive values of Granules of Majoon Aarad Khurma was found to be 4.2 ± 0.11 in Petroleum Ether, 0.73 ± 0.06 in Chloroform, 19.13 ± 0.17 in Ethyl-alcohol and 37.2 ± 0.23 in water. The Successive Extractive values of the drugs were determined. When the values were compared with values of MAK mentioned in physico-chemical standard of Unani Medicine by CCRUM the values of GMAK were higher than the values of MAK. This indicates the efficacy of GMAK is higher than MAK [35].

pH of the drug were determined and was found to be acidic for each drug the values being 5.82 ± 0.008 in 1 % aqueous solution and 5.27 ± 0.008 in 10 % aqueous solution of Granules of Majoon Aarad Khurma. The **pH value** of various dosage forms of plant drugs may also be considered a parameter for the purity of a drug. The pH and hydronium ion concentration also play an important role in the study of drug receptor-site interactions, an area of research which has gained considerable impetus during recent years [36, 37].

The **bulk density, tapped Density, Carr's index and Hausner ratio** of Granules of Majoon Aarad Khurma found to be, 0.56 gm/ml, 0.65 gm/ml, 12%, and 1.12 respectively [36]. **Bulk density** of a compound varies substantially with the method of crystallization, milling, or formulation.

Compressibility Index and the Hausner's ratio are the simple, fast and popular methods of predicting powder flow characterstics, the compressibility index has been proposed as an indirect measure of bulk density, size and shape, surface area, moisture content and cohesiveness of materials.

The percentage of Ash values of Granules of Majoon Aarad Khurma were found to be 2.5 ±0.28 total ash, 0.66 ± 0.16 acid insoluble ash and 1.16 ± 0.16 water soluble ash .**Ash value** is the residue that remains after complete incineration of the drug. Ash value plays an important role in ascertaining the standard of a drug, because the dust, earthy and unrequired matters are generally added for increasing the weight of a drug resulting in the higher ash percentage. Therefore, the ash value determination furnishes the basis of judging the identity and cleanliness of a drug and gives information related to its adulteration with inorganic matter. [38]

TLC studies of Alcoholic extract of the test drug Granules of Majoon Aarad Khurma was performed and R_f values of various spots appeared in Toluene: Ethyl acetate (7: 3, with 2 drop sulphuric acid) solvents system was found to be 0.31, 0.36, 0.50, 0.68, 0.75 respectively. In GMAK five spots were observed. [39, 40].

Thin layer chromatography is one of the important parameter used for detecting the adulteration for judging the quality of the drugs. If the drug is adulterated there might be appearance of the other compounds present in adulterant, in turn may increase the no. of spots. On the other hand the exhausted or deteriorated drugs may lose the component and the number of spots appeared might be less.

Physico-Chemical data of GMAK

Sl. No	Physico Chemical Properties	GMAK
1.	Organoleptic properties Apearance Odour Smell Taste	 Granules Brownish Pleasant Sweet
2.	Water Soluble Matter	36.6%
3.	Successive Extractives Petroleum Ether Chloroform Ethyl Alcohol Aqueous	 4.2% 0.6% 19.13% 37.2
4.	PH Value 1% 10%	 5.82 5.27
5.	Ash Value Total Ash Acid Insoluble Ash Water Soluble Ash	 2.5% 0.66% 1.16%
6.	Bulk Density Tapped Density Carr's Index Hausner Ratio	0.6gm/ml 0.68gm/ml 12% 1.13
7.	TLC Rf Values	0.31 0.36 0.50 0.68 0.75

TLC plates high lighting the spots in GMAK

CONCLUSION

The present study was aimed to modify the Unani Aphrodisiac formulation Majoone Aarad Khurma into the granular form with *Stevia*, a natural sweetening agent instead of sugar as a base in Majoon. *Stevia* also possess the action of lowering the glucose level. Therefore the Granules of MAK which contain *Stevia* will serve as a good aphrodisiac as combination of both these will be beneficial for the diabetics having the sexual dysfunction.

The Physicochemical standards for scientific evaluation of granules of Majoon Aarad Khurma were estimated and the standards were evaluated as recommended by CCRUM.

Based on the finding it is concluded that:

- Granules possessed the same principles and maintained same characteristics as traditional dosage form Majoon Aarad Khurma.
- The granules of Majoon Aarad Khurma were found to be more stable, convenient and comfortable in usage and dispensing, and also safe, light, efficacious, cost effective and quality controlled.
- Stevia a natural sweetening agent which was used as base for granules has been previously reported to be non toxic (Hamdard Stevia) hence Stevia can be used as safe and efficacious sweetening agent in preparation of granules as well as in other Unani formulations.
- *Stevia* also possess the action of lowering the glucose level. So it can be used for erectile dysfunction in diabetic patients.
- When the values were compared with values of MAK mentioned in physico-chemical standard of Unani Medicine by CCRUM the values of GMAK were higher than the values of MAK. This indicates the efficacy of GMAK is higher than MAK [41].

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