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Original Article

Formulation and Physicochemical Evaluation of *Joshanda* (*Decoction*) *Munzije Balgham* as Granules

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ABSTRACT

Background: *Joshanda* (decoction) is an effective dosage form in Unani System of Medicine but its unpalatable taste and preparation creates difficulty in patient compliance. *Joshanda* when freshly prepared has a very short shelf life. Thus, the modified dosage form like granules can fulfill these drawbacks and withstand the need of contemporary life style as a ready to use and in portable form. In this study, an attempt was made to modify *Joshanda Munzjie Balgham* (JMB) into contemporary granule dosage form with the help of suitable permissible excipients. **Materials and Methods:** JMB. was prepared by classical method and dried in Rotary evaporator followed by complete drying on water-bath. The extract was then mixed with required excipients to form the granules by wet granulation technique. The modified granules and JMB were subjected to various physico-chemical analysis, qualitative and quantitative estimation of phytoconstituents, GCMS, Microbial count, LCMS and HPTLC. *Joshanda Munzije Balgham Granules* (JMBG) were also subjected to stability study with accelerated conditions of temperature 40±2ºC and relative humidity 75±5ºC for three months. **Results:** From one dose of JMB, 28% extract yield percentage was obtained which was successfully converted into fast dissolving JMBG with various excipients. Qualitative analysis of granules confirmed the presence of various phytoconstituents. Quantitative estimation by spectrophotometric method showed the presence of total concentration of Phenols, Tannins, Glycosides, Flavonoids, and Alkaloids as 157.51, 22.35, 2.25, 98.68 and 195.5 µg/mL respectively. GCMS data displayed total 31 peaks in JMB, 8 in JMBG and 8 in JMBG (3rd month). LCMS data for JMBG displayed 28 constituent peaks. HPTLC fingerprinting carried out in two mobile phases reported the highest number of peaks in in toluene; ethyl acetate: formic acid (5:4:1). JMB Granules were found to achieve shelf life of one year on set parameters. The chemical constituents found by qualitative and quantitative analysis and chromatography of JMB and JMBG were comparative. **Conclusion:** This work can help in improving the shortcomings of traditional *Munzije Balgham Joshanda* to some extent and make it portable, palatable and increases its shelf life.

Keywords: Decoction, Fast dissolving Granules, *Joshanda Munzije Balgham*, Wet Granulation.

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INTRODUCTION

Joshanda (Decoction) is one of the many fundamental and highly effective classical compound formulations mentioned in the Unani system of medicine like *Safoof* (powder), *Khesanda* (infusion), *Majoon* (semi solid dosage form), *Arq* (distillate), *Marham* (ointment), *Zimad* (paste) etc. Decoction known as *Joshanda* in Persian and *Kaadha* in Hindi, *Matbookh* or *Tabeekh* in Arabic, is defined as a homogenous and pure fresh liquid dosage form, obtained when one or more drugs are soaked in water or any Arq (Distillate) for overnight and boiled, filtered and taken in the morning or as indicated. The drug water ratio in it can be of 1:3, 1:5, 1:6 or 1:8. It should be boiled as indicated until water remains half or one third.[1-3]

As the dosage form plays important role in patient and drug regime compliance, availability of drug in different dosage forms is important to increase the worldwide acceptability of Unani/ traditional system of medicine. *Joshanda* as a dosage form is much effective but has drawbacks as well. Its unpalatable taste makes it difficult for the patient to consume and comply. So, there is immense scope and need to modify these classical dosage forms as maintenance of correct dose every time is difficult otherwise. *Joshanda* is prepared fresh every time before use as it has very short shelf life, and is easily affected by micro-organism. Therefore, emphasis can be made for the need to change the conventional Unani dosage form into a readily available and effective form like granules which may retain the advantages of decoction and thus

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eventually help in the easy dispense, availability, preparation and consumption of medicine.

Joshanda Munzije Balgham (JMB) taken in this study for modification, is an important Unani Classical pharmacopeial dosage form and the suffix which is added to *Joshanda* is attributed to the dominant action of drugs that it carries out. As the *Joshanda Munzije Balgham* name indicates, it causes *Nuzj* i.e, concoction of the *Balghami madda* through the action of *Munzije Balgham* drugs that it is comprised of. The literal meaning of Nuzj is "*pakana*" i.e processing of *madda-e-maraz* (causative matter).[4]

In medical physiology, Hippocrates is credited with developing the concept of the "four humours" *Balgham* (phlegm), *Safra* (yellow bile), *Sauda* (black bile), and *Dam* (blood).[5]

Al Razi (865- 925 AD) also gives special emphasis on treatment of cases according to their type in relation to the dominating khilt.[6] *Munzije Balgham* is thus indicated in most of the chronic diseases which occur due to the accumulation of *Balgham* in the body and are predominant nowadays, like *Nazla, Zukaam* (cold and flu), *Khansi* (Cough), *Laqwa* (facial palsy), *Falij* (Hemiplegia), *Istarkha* (Flaccidity), *Khaddar* (numbness), and Joint diseases like *Wajaul Mafasil* (Arthritis), *Nuqras* (Gout), *Irqun-nissa* (Sciatica) etc. *Joshanda Munzije Balgham* formulation is indicated in all these diseases with a little variation of combination.[7] Hence knowing the importance and wide range of application of this classical dosage formulation of *Joshanda Munzije Balgham* (JMB), an attempt was made to convert JMB into fast soluble granules with suitable permissible excipients, in order to overcome the shortcomings of JMB and make them much trendy, ready to use, effective and palatable for the patients. Comparative analysis of JMBG with classical decoction was also made in.

Ingredients of Joshanda Munzije Balgham

Badiyan (*Foeniculum vulgare* Mill), Bekh Badiyan (Root of *Foeniculum vulgare* Mill), Bekh kasni (*Cichorium intybus* Linn.), Bekh Karafs (*Apium graveolens* Linn.), Bekh Izkhar (*Andropogon jwarancusa* Schult), Ustukhudoos (*Lavendula stoechas* Linn.), all 7 g.; Aslulsoos muqashir (*Glycyrrhiza glabra* Linn.) 5 g; Mawaiz Munaqqa (*Vitis vinifera* Linn.) 9 in number, Anjeer (*Ficus carica* Linn.) 5 in number, Parsiooshan (*Adiantum capillus-veneris* Linn.) 7g. This formulation is selected from *Al Qarabadeen* and *Qarabadeen* Azam.[1,8] Both texts are part of first schedule of Drug and Cosmetic act.[9] The same formulation is also mentioned in *Jamia ul Hikmat*.[10]

MATERIALS AND METHODS

Out of 10 ingredients of JMB, nine were procured from the pharmacy of National Institute of Unani Medicine (NIUM) and one drug i.e Parsiooshan (*Adiantum capillus*-veneris) was procured from outside store i. e. Sana Herbals Bangalore. All the 10 drugs were authenticated from Central Ayurveda Research Institute, Bangalore, with their respective accession numbers as *Glycyrrhiza glabra* Linn (Ref. RRCBI mus- 149), *Foeniculum vulgare* Mill and Root of F.V Mill (Ref. RRCBI mus- 145), *Cichorium intybus* Linn. (Ref. RRCBI mus- 262), *Apium graveolens* Linn. (Ref. RRCBI mus- 289), *Andropogon jwarancusa* (Ref. RRCBI mus- 307), *Lavendula stoechas* Linn. (Ref. RRCBI mus- 304), *Vitis vinifera* Linn. (Ref. RRCBI mus- 125), *Ficus carica* Linn. (Ref. RRCBI mus- 17613), *Adiantum capillus-veneris* Linn. (Ref. RRCBI mus- 303). All the drugs were also deposited in NIUM museum repository with voucher specimen no. 129/IS/Res/2022.

All the chemicals, solvents, excipients and instruments used in this study were availed and study was performed in laboratory of Department of Ilmul Saidla (Pharmacy) NIUM and few tests were outsourced.

Preparation of *Joshanda Munzije Balgham* (JMB) by classical method

JMB was first prepared by classical method as mentioned in Unani literature. To prepare JMB, all the ingredients of the formulation were cleaned and crushed to smaller pieces (*neem kofta*) with the help of mixer grinder, to get maximum efficacy of the formulation. All the drugs (100 g.) were soaked in 800 ml of water (1:8 ratio) overnight. In the morning, the mixture was boiled with closed lid until 1/3 water was left. One dose of prepared JMB contains 270 mL decoction. The mixture was then strained with the help of muslin cloth (fabric with warp 22 per cm±1 and weft 18±1 per cm) and the final filtrate was collected and processed further to make granules.[1,11,12]

Formulation of Granules from JMB

Preparation of non-native extract

After carrying out different methods for checking highest extract yield percentage, rotary evaporation was selected as the most suitable initial method of drying due to highest yield percentage with minimum possible direct heat exposure in order to avoid degradation of volatile constituents and also being commercially feasible. JMB (270 mL) prepared by classical method was added with 10% Maltodextrin (MTD) (10% of weight of crude drugs) and was mixed well. Maltodextrin was used for ease of scrapping and powdering of the extract, which was difficult when tried without that. It was then filled in 1000 mL borosilicate buchi type flask of rota-evaporator. The drying was carried out at 65°C with 60 RPM for 60 min till the JMB was converted into thick consistency liquid which was then removed and transferred into a stainless-steel tray and was completely dried on water bath at 60-65°C. The extract was finally scrapped off and stored in airtight jars for further processing.

Granulation

One dose of non-native extract i. e. 38 g. obtained from 100 g. drugs, (28 g. native extract and 10 g. maltodextrin) was powdered with the help of mixer grinder and was mixed with various excipients, in different combination and different ratios till the desired ideal granule parameters were achieved. All the excipients were sieved before mixing and weighed accurately using digital weighing balance. The excipients used while making the different granule batches are: Soluble starch, Lactose, Aerosil, SSG., MCC., Magnesium stearate, Mannitol, Sugar, Methyl and Propyl parabens, Sodium benzoate, 10% Aslulsoos drug powder, 10% Mawaiz and Anjeer paste and different flavors like Clove, Vanilla, Menthol and their combinations. Different batches of the granules were prepared on trial-and-error basis by wet granulation technique. Some batches of the granules were tried without using sugar and rest of the batches were made with sugar. The sugar ratio attempted was one part, two parts and three parts and it was tried in increasing order to increase the palatability of granules. The other excipients were also mixed in different ratios to get the desired parameters. 16 batches of granules were made in total and the final batch *i. e.* batch 16 (B16) was selected for further evaluation on the basis of colour, palatability, solubility and flowability of granules. Detail of total batches prepared and excipients used is depicted in Table 1.

Stepwise formulation of granules from non-native extract of JMB

Step 1: The extract was mixed with well sieved excipients and was powdered. In batches 1-5 sugar was not used but in all the other batches extract was mixed with powdered sugar along with excipients. The geometrical method of mixing was followed with the help of small mixer jar to simulate R.M.G. **Step 2:** The powdered mixture was then sprayed with 9-10 ml of water and ethanol in 50:50 ratio, 10 to 12 sprays were used for one batch and was mixed properly until a damp mass was formed which was then passed through the granulator (Cemach granulator, oscillating type 8-inch GMP Model, M/CNo. 1417) with sieve no.16 # in it and the wet granules were collected in a steel tray for further processing. The hydro-alcoholic liquid was used due to highly hygroscopic nature of the extract. **Step 3:** The granules thus collected were dried in hot air oven (labline Mod. No. HO 6.7) at 60°C for 90 min. The temperature and time of drying was kept constant for all the batches. **Step 4:** After cooling the granules were mixed with Aerosil, Magnesium stearate and

Table 1: All batches of granules prepared with different excipients in varying ratio.

Sl. No.	Extract (wt.in gm)	MTD (wt. ing)	Sod. Benz %	Starch %	Lactose%	MCC%	Aerosil%	Magnesium stearate %	Mannitol %	SSG%	Methyl:propyl parabens	Drug pdr/ pst%/ flavour	Sugar in parts
1	28	10	0.15	-						2			No sugar
2	28	10	0.15	-						2		10% pdr	-
3	28	10	0.15	10						2			-
4	28	10	0.15	10						2		10%pdr.	-
5	28	10	0.15	20	20	5				2			-
6	28	10		10			0.25			2	0.06:0.03		1
7	28	10		10	20	5	0.25			4	0.06:0.03	Clove	2
8	28	10		20			0.25			2	0.06:0.03	Vanilla	2
9	28	10		10			0.25	0.25		2	0.06:0.03	Menthol	2
10	28	10		10			0.25	0.25		2	0.06:0.03		3
11	28	10		10			0.25	0.25		2	0.06:0.03	10% pst. Anj. & mwz.	3
12	28	10		10			0.5			2	0.06:0.03	Vanilla	3
13	28	10		10			0.25	0.25		2	0.06:0.03	Menthol	3
14	28	10		10			0.25	0.25		2	0.06:0.03		4
15	28	10		10			1	0.5		2	0.06:0.03	Menthol	4
16	28	10		10			2	0.5	10	2	0.06:0.03	Menthol	3

*MTD = Maltodextrin; Sod.Benz = Sodium Benzoate; MCC = Microcrytalline cellulose; SSG = Sodium Starch Glycolate; pdr = Powder; pst = Paste; Anj. = Anjeer; Mwz = mawaiz.

powdered menthol crystals. Clove and Vanilla flavor and their combinations were also tried in different batches to achieve the best possible and acceptable flavor. **Step 5:** Granules were then stored in airtight glass bottles with silica gel pouches within it and were evaluated for different parameters. Ideal batch was selected on set parameters such as color, taste, solubility time, and flow properties and was subjected to further qualitative and quantitative tests.

Packing of granules

One complete dose of final batch of formulated dried granules i. e.132 g. (extract and excipient) was packed in two triplex gold standing pouches (purchased from color flex foils and pouches Bangalore, having 100 g. capacity each with dimensions of 100 mm x 170 x 35), in two equal divided doses with each pouch carrying 66 g. of granules (Figure 1). The triplex gold standing pouches were three layered pouches, which provided high barrier protection against oxygen, moisture and UV rays. The pouches were re-usable and zip locked. The triple layer pouches were sealed with the help of paddle sealing machine, model Pack-o-matic, PACTEC India at NIUM Pharmacy.

Evaluation of formulated *Joshanda Munzije Balgham* Granules (JMBG)

Organoleptic parameters

Color, taste, odour and texture of the granules was analysed. pH value of 1% and 10% solution. Total solid content of JMBG was calculated. In Granules characterization, tapped density, angle of repose, Bulk density, Compressibility index or Carr's index, and Hausners ratio were calculated.[13-17]

Loss of weight on Drying (LOD) at 105°C, Moisture content by Toluene Distillation (TD) method, Ash values i.e. Total ash, Acid insoluble ash, Water soluble ash Extractive values viz Successive extractive values, non-successive extractive values, Alcohol soluble extractive values, Water soluble extractive values were calculated.[12-14,18-21]

Qualitative analysis of granules

Qualitative analysis of JMBG was carried out to confirm the presence of alkaloids, flavonoids, tannins, saponins, glycoside, phenols, carbohydrates (Fehlings test, Anthrone test and Benedicts test) and steroids - Salkowski reaction.[19,22,23]

Quantitative analysis of granules by spectrophotometric analysis

Quantitative estimation of phytochemicals was carried out with the help of Dextrose Technologies Pvt. Ltd., Bangalore for the determination of Total Phenolic content**,** Total Flavonoid, Total Tannins, estimation of Glycosides and Total Alkaloid content.[24-27]

Quantitative analysis of granules by weight measurement (percentage determination)

Determination of Alkaloids, Flavonoids, and Tannins was also carried out by weight measurement.[28]

Microbial contamination test

Microbial Load analysis was also done with the help of Dextrose Technologies Pvt. Ltd., Bangalore. The test was performed according to Pharmacopoeia to ensure sterility of the preparations. The test for sterility was carried out under aseptic conditions using direct inoculation method.[29]

GC-MS (Gas Chromatography–Mass Spectrometry) Analysis with NIST of granules

GCMS was done at Skanda life Sciences Pvt. Ltd., Bangalore. The sample was subjected to GCMS and the total separated peaks were recorded. Extracted ion chromatograms were obtained from all the major peaks. The mass spectrum of the unknown component was compared with the spectrum of the known components stored in the NIST library Instrument used – GC/MS Clarus 500 (Perkin Elmer); Column – RestekRtxR – 5, (30-m X 0.25 mm) (5% diphenyl/95% dimethyl polysiloxane); Oven Temp. – Initial temp: - 40°C for 5 min; Ramp 1: - 6°C/min to 280°C, - 280°C for 15 min; Injector Temp: - 280°C; Injection Volume: - 1.0 µL; Run time: - 60 min.[30]

LC-MS (Liquid Chromatography–Mass Spectrometry) Analysis

Carried out with the help of Dextrose Technologies Pvt. Ltd., Bangalore. The LC-MS analysis of aqueous fraction was performed using a Waters Mass Q-TOF Mass Spectrometer with diode array detector.[31]

High Performance Thin Layer Chromatography

HPTLC was executed with the help of PES college of pharmacy, Bangalore; Instrument: CAMAG Linomat 5; Sample preparation: 2.5 g of each given samples was dissolved in 5 mL of distilled water and HPTLC grade methanol and all the samples were kept in sonicator to achieve maximum solubility. Sample solvent type: 1) aqueous 2) methanolic; Stationary phase: TLC Aluminium sheet silica gel 60F 254 by E. MERCK KGaA Germany; Mobile phases used: 1) toluene: ethyl acetate in 9.3:0.7 ratio. 2) toluene: ethyl acetate: formic acid 5:4:1 ratio; Wavelength: 1) 254 nm. 2) 366 nm; Spray gas: inert gas, Dosage speed: 150 nl/s, Pre dosage volume: 0.2 ul; Syringe size: 100 ul; Number of tracks: 12; Sample ID 1-4: Pure extract (Aqueous/ methanolic); Sample ID 5-8: Formulation (granules); Sample ID 9-12: Excipients only. Application position Y: 8mm, Band length: 8mm.[32]

Stability testing

The packed and sealed granule pouches were kept in stability chamber with proper labeling of name of the formulation, date of preparation of granules, date of commencement of thermal and humidity exposure and date of withdrawal on the pouch. Thermal and humidity challenge was carried out for three months. Short term accelerated stability testing was carried out at elevated temperature and humidity conditions of 40°C±2°C with Relative Humidity of 75%±5% RH according to ICH guidelines in Stability chamber and was accessed as per API guidelines.[33-36]

Figure 1: Joshanda Munzije Balgham Granules packed in Triplex foil sachets.

RESULTS

Formulation of granules

Fast dissolving granule was formulated and final selected batch of JMB Granules (JMBG) contains combination of 28 g pure extract, 7.67% MTD, 10% Starch, 10% Mannitol, 2% SSG, 2% Aerosil, 0.5% Magnesium stearate, 0.06:0.03% Methyl: Propyl parabens as preservative and 0.2% powdered Menthol crystals as flavor and three parts sugar (84 g.) (Table 1). It displayed Solubility time of 36 sec in luke warm water and was of light brown colour with good palatability by mint flavor.

Qualitative analysis of granules (JMBG)

Qualitative analysis of granules of JMBG confirmed the presence of Flavonoids, Alkaloids, Saponins, Tannins, Glycosides, Phenols, Terpenoids, Carbohydrates and Mucilage. The results of all the physicochemical parameters assessed are depicted in tabulated form in Tables 2 and 3.

Table 2: Comparative data of Granules (JMBG) and Joshanda (JMB).

Parameter	Granules (JMBG)	Joshanda (JMB)
Organoleptic characteristics		
Colour	Light brown	Dark amber colored
Taste	Sweet and mint	Bitter and acrid
Odour	Strong Mentholic	Pungent
Texture	Free flowing	Mucilaginous
pH value		
1%	6.25±0.03	6.5±0.08;
10%	5.64±0.005	5.7±0.08
Ash value		
Total ash	1.8±0.11	5.6±0.008
Acid insoluble	0.76±0.14	0.66±0.16
Water soluble	1.16±0.17	4.44±0.44
Total solid content		
TSC	51.5±0.98	12.53±0.17
Total mucilage content		
TMC	1.01±0.04	1.16±0.14
Quantitative estimation of phytoconstituents by spectrophotometric method (µg/L)		
Phenols	157.51	162.49
Tannins	22.35	26.29
Glycosides	2.25	2.28
Flavonoids	98.68	123.07
Alkaloids	195.5	256.29

Microbial contamination test

Sterility test showed total microbial count of JMBG as 1.2×10^2 CFU/g. No growth of specific pathogen such as *E. coli, S. aureus* and *P. aeruginosa* and *S. typhi.* was found (Figure 2).

Chromatography

Gas Chromatography Mass Spectrometry (GCMS) with NIST

The reported GCMS peaks with NIST of JMBG and JMB are depicted in Figures 3 and 4.

Liquid Chromatography Mass Spectometry (LCMS) Analysis

The peaks and graphs with retention time and area % recorded in LCMS of JMB Granules are depicted in Figure 5.

Table 3: Physico-chemical analysis and microbial load of JMBG.

Parameter	Mean %
Granule characteristics of JMBG	
Angle of repose	26.34±0.56
Bulk density	0.66±0.006
Tapped density	0.76±0.01
Hausners ratio	12.33±0.18
Carr's index	1.14±0.03
Microbial load of JMBG	
Total bacterial count	1.2×10^2
Total fungal count	No growth
E coli, Salmonella, S. aureus, Pseudomonas	No growth
Successive extractive value	
Pet ether	0.53±0.08
Benzene	0.37±0.01
Chloroform	0.19±0.01
Ethanol	24.43±0.28
Water	69.83±0.16
Non-Successive extractive value	
Pet ether	0.46±0.03
Benzene	0.77±0.01
Chloroform	0.35±0.02
Ethanol	38.29±0.20
Water	92.73±0.43
Alcohol Soluble Extractive Value (ASEV)	
ASEV	2.07±0.13
Water Soluble Extractive Value (WSEV)	
WSEV	26.53±0.59
Moisture content	
L. O. D	3.1± 0.05
T. D	2.76± 0.17%

High Performance Thin Layer Chromatography (HPTLC)

TLC plates were developed using two different solvents i.e. water and methanol in two different mobile phases i.e. Toluene: Ethyl acetate (9.3: 0.7) (M1) and Toluene: Ethyl acetate: Formic acid (5:4:1) (M2). The finger prints were recorded. HPTLC Densitometric chromatogram of the pure extract, granules and excipients scanned at UV-254 and 366 nm are displayed in Figures 6 and 7, (Table 4).

In M2 -Track 4, pure extract was dissolved in water and visualized at UV-254 at application volume 8.0 µL displayed 7 constituent peaks, in which peak no. 5 at R_f 0.46 displayed highest area percentage of 32.63% showing highest unknown constituent in pure extract. When visualized at UV 366 displayed 10 peaks. In M2-Track 8, granules dissolved in water and visualized at UV-254 at application volume 8.0 µL also displayed 4 constituent peaks. In this peak no.3 at R_f 0.61 exhibited highest area percentage of 41.05% showing highest unknown constituent and when visualized at UV 366 displayed 8 peaks. In M2-Track 12, excipients dissolved in water and visualized at UV-254 at application volume 8.0 µL exhibited 4 excipients peaks, in this peak no.3 at R_f 0.69 displayed highest area percentage of 58.29% showing highest unknown excipient constituent. When visualized at UV 366 displayed no peaks. (Figure 6) In M2-Track 4, pure extract sample when dissolved in methanol, visualized at UV-254 at application volume 8.0 µL displayed 8 constituent peaks, in this peak no.4 at R_f 0.29 showed highest area percentage of 32.05% displaying highest unknown constituent in pure extract. When visualized at UV 366 displayed 11 peaks in track 2. In M2-Track 8, granules dissolved in methanol visualized at UV-254 at application volume 8.0 µL also displayed 11 constituent peaks, in this peak no. 9 at R_f 0.47 displayed highest area percentage of 36.61% showing highest unknown constituent and when visualized at UV 366 displayed

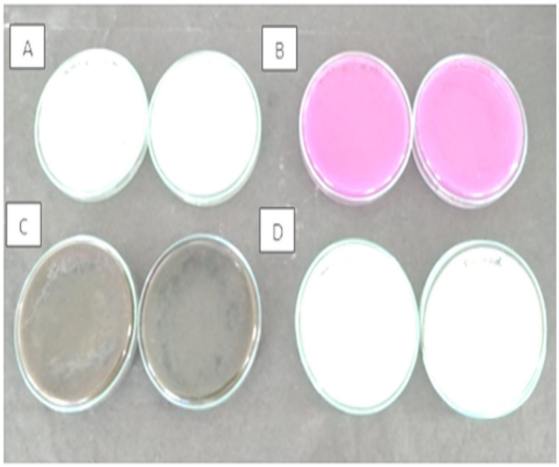
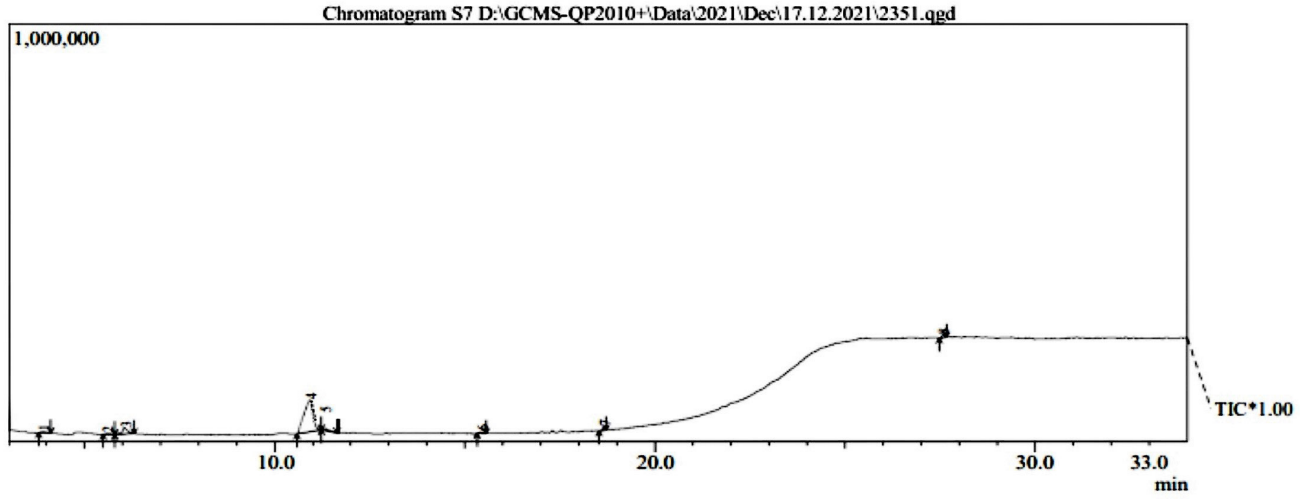


Figure 2: Sterility test results- A- Choromogenic agar plates, B- Rose Bengal agar plates C- Eosin methylene blue agar plates, D- plate count agar plates.

Sample Information

Analyzed by	: Admin
Analyzed	: 12/21/2021 2:26:28 PM
Sample Type	: Unknown
Level #	1
Sample Name	: S7
Sample ID	2351
IS Amount	: [1]=1
Vial #	52
Injection Volume	1
Data File	: D:\GCMS-QP2010+\Data\2021\Dec\17.12.2021\2351.qgd
Org Data File	: D:\GCMS-QP2010+\Data\2021\Dec\17.12.2021\2351.qgd
Method File	: D:\GCMS-QP2010+\Ullas\IADFAC SCAN.qgm
Org Method File	: D:\GCMS-QP2010+\Ullas\IADFAC SCAN.qgm



Peak Report TIC

Peak#	R.Time	I.Time	F.Time	Area	Area%	Name
1	3.873	3.783	4.117	37062	2.34	1,2-Cyclopentanedione
2	5.589	5.483	5.792	20592	1.30	4-Oxononanal
3	6.042	5.792	6.308	145563	9.18	2-Heptanamine, 5-methyl-
4	10.923	10.575	11.225	1247955	78.69	1,3-Propanediol, 2-(hydroxymethyl)-2-nitro-
5	11.313	11.233	11.642	44091	2.78	3,4-Altrosan
6	15.433	15.325	15.558	22293	1.41	Trichloroacetic acid, tridec-2-ynyl ester
7	18.650	18.525	18.725	31374	1.98	2,6-Di(2-furylmethylidene)cyclohexan-1-one
8	27.572	27.483	27.658	37037	2.34	.beta.-Sitosterol
				1585967	100.00	

Figure 3: GCMS graph with NIST - Peak Report TIC of Granules (JMBG).

8 peaks in track 8.In M2-Track 12, excipients when dissolved in methanol and visualized at UV-254 at application volume 8.0 µL exhibited 7 excipients peaks, in this peak no 6 at R_f 0.46 displayed highest area percentage of 56.78% showing highest unknown excipients, when visualized at UV 366 displayed one peak (Figure 7).

Stability study data

GCMS with NIST-GCMS Peak report of JMBG at three month (stability study) is depicted in Figure 8. Other physico-chemical parameters of stability data at 0 and 3 month is depicted in Table 5.

DISCUSSION

The efficacy of *Joshanda Munzije Balgham* (JMB) is well mentioned in the literature of Unani medicine. According to *Jalinoos, Balgham* closely resembles blood and plays the role whenever there is need. It also provides nutrition to the body organs whenever the blood becomes deficit to meet those needs.[6] Therefore any imbalance in Balgham leads to occurrence of many diseases which can be treated with the *Munzije Balgham drugs* and its formulations like JMB. The aim of the present study was to make JMB ready to use, effective, portable and palatable. JMB was decocted and converted in soluble granules. The combined aqueous extract of the drugs was taken to simulate the classical method of preparation of decoction. Batch 16 (B16) having three

Analyzed by	: Admin
Analyzed	: 3/4/2022 12:37:30 PM
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Level #	: 1
Sample Name	: Jashanda New
Sample ID	: 2838
IS Amount	: [1]=1
Vial #	: 6
Injection Volume	: 1
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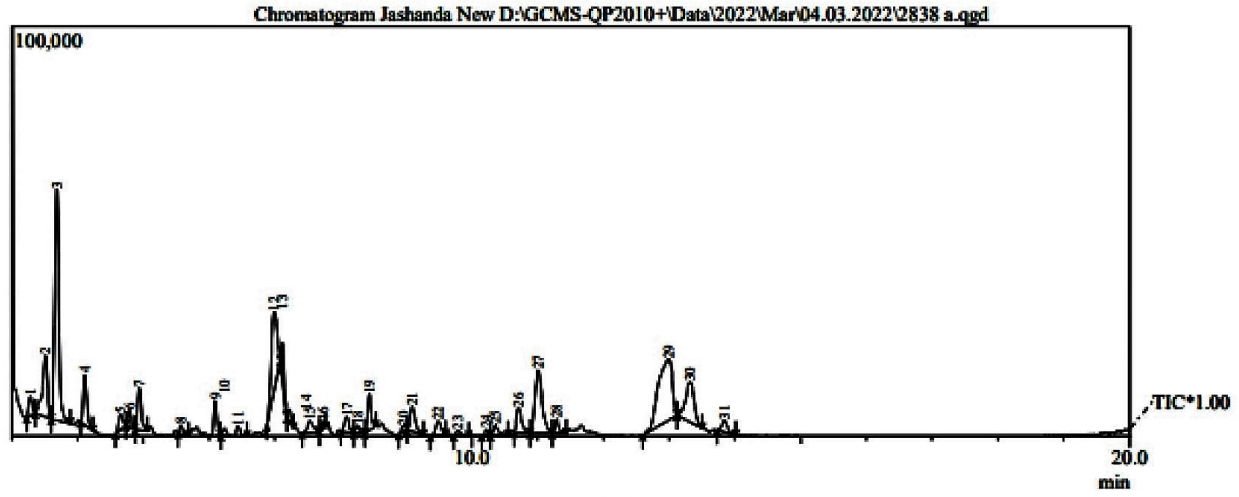
Method File	: D:\GCMS-QP2010+\Ullas\IADFAC SCAN Split 25.qgm
Org Method File	: D:\GCMS-QP2010+\Ullas\IADFAC SCAN Split 25.qgm



Peak Report TIC

Peak#	R.Time	I.Time	F.Time	Area	Area%	Name
1	3.283	3.225	3.358	16512	1.26	2-Furanmethanol
2	3.515	3.358	3.600	78019	5.97	Butanoic acid, 2-ethyl-3-oxo-, methyl ester
3	3.687	3.600	3.892	237453	18.16	dl-Glyceraldehyde dimer
4	4.110	4.050	4.233	46529	3.56	1,2-Cyclopentanedione
5	4.658	4.575	4.733	17132	1.31	Glycerin
6	4.792	4.733	4.867	13825	1.06	1,3-Dioxane, 4-methyl-
7	4.940	4.875	5.067	39949	3.06	2-Propen-1-ol
8	5.572	5.525	5.683	6859	0.52	1,3-Dioxol-2-one,4,5-dimethyl-
9	6.096	6.025	6.175	30160	2.31	Cyclopentane, 1-acetyl-1,2-epoxy-
10	6.234	6.183	6.358	8161	0.62	2,2'-Bioxirane, (R*,R*)-(.+/-.)-
11	6.442	6.358	6.583	12396	0.95	Pentanal
12	6.991	6.883	7.083	121000	9.25	Propanal, 2,3-dihydroxy-, (S)-
13	7.117	7.083	7.175	22059	1.69	4H-Pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl-
14	7.222	7.183	7.292	8491	0.65	2(3H)-Furanone, dihydro-4-hydroxy-
15	7.535	7.417	7.683	17178	1.31	(S)-5-Hydroxymethyl-2[5H]-furanone
16	7.735	7.683	7.775	5548	0.42	(S)-(+)-2',3'-Dideoxyribonolactone
17	8.096	8.008	8.200	18009	1.38	Cyclopentanol, 2,4,4-trimethyl- $$ 2,4,4-Trimethylcyclopentanol
18	8.258	8.200	8.367	7418	0.57	2-Furancarboxaldehyde, 5-(hydroxymethyl)-
19	8.440	8.367	8.533	31627	2.42	1,2,3-Propanetriol, monoacetate
20	8.959	8.883	9.008	5386	0.41	4H-Pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl-
21	9.092	9.008	9.267	31805	2.43	1-Deoxy-d-altritol $$ 1-Deoxyhexitol
22	9.486	9.367	9.600	19198	1.47	2-t-Butyl-5-methyl[1,3]dioxolan-4-one
23	9.787	9.717	9.958	7982	0.61	Pentanoic acid, propyl ester $$ Valeric acid, propyl ester
24	10.221	10.150	10.283	5659	0.43	1,2-Butanediol, 3,3-dimethyl-
25	10.354	10.283	10.550	14625	1.12	Isooctanol
26	10.710	10.642	10.883	31673	2.42	2,3,4,4-Tetramethyl-pentane-1,3-diol
27	11.007	10.883	11.217	113243	8.66	Sucrose $$ .alpha.-D-Glucopyranoside, .beta.-D-fructofuranosyl
28	11.288	11.217	11.433	14396	1.10	Benzoic acid, 3-hydroxy-, methyl ester
29	12.990	12.600	13.125	220787	16.88	3-Deoxy-d-mannoic lactone
30	13.318	13.125	13.500	87506	6.69	3-Deoxy-d-mannoic lactone
31	13.840	13.725	14.017	17056	1.30	.alpha.-d-Mannofuranoside, methyl
				1307641	100.00	

Figure 4: GCMS graph with NIST - Peak Report TIC of Joshanda (JMB).

parts of sugar was selected as the final batch, which achieved the desired parameters like colour, good taste, texture, solubility time etc. The colour of granules varied after addition of each part of sugar like granules having one part of sugar were dark brown in colour while as granules with three parts were lighter in colour. MTD was used to prepare nonnative extract which fascilitated scrapping, drying and powdering of extract.[37] Sodium Starch Glycolate (SSG), Starch and Mannitol were used to enhance disintegration time, as antiadhesive and diluents.[38] Magnesium stearate was used as anti-caking agent and Aerosil 200 was employed in the formulation as a moisture scavenger and Glidant.[38,39] The different concentrations of Aerosil and Magnesium Stearate were used to

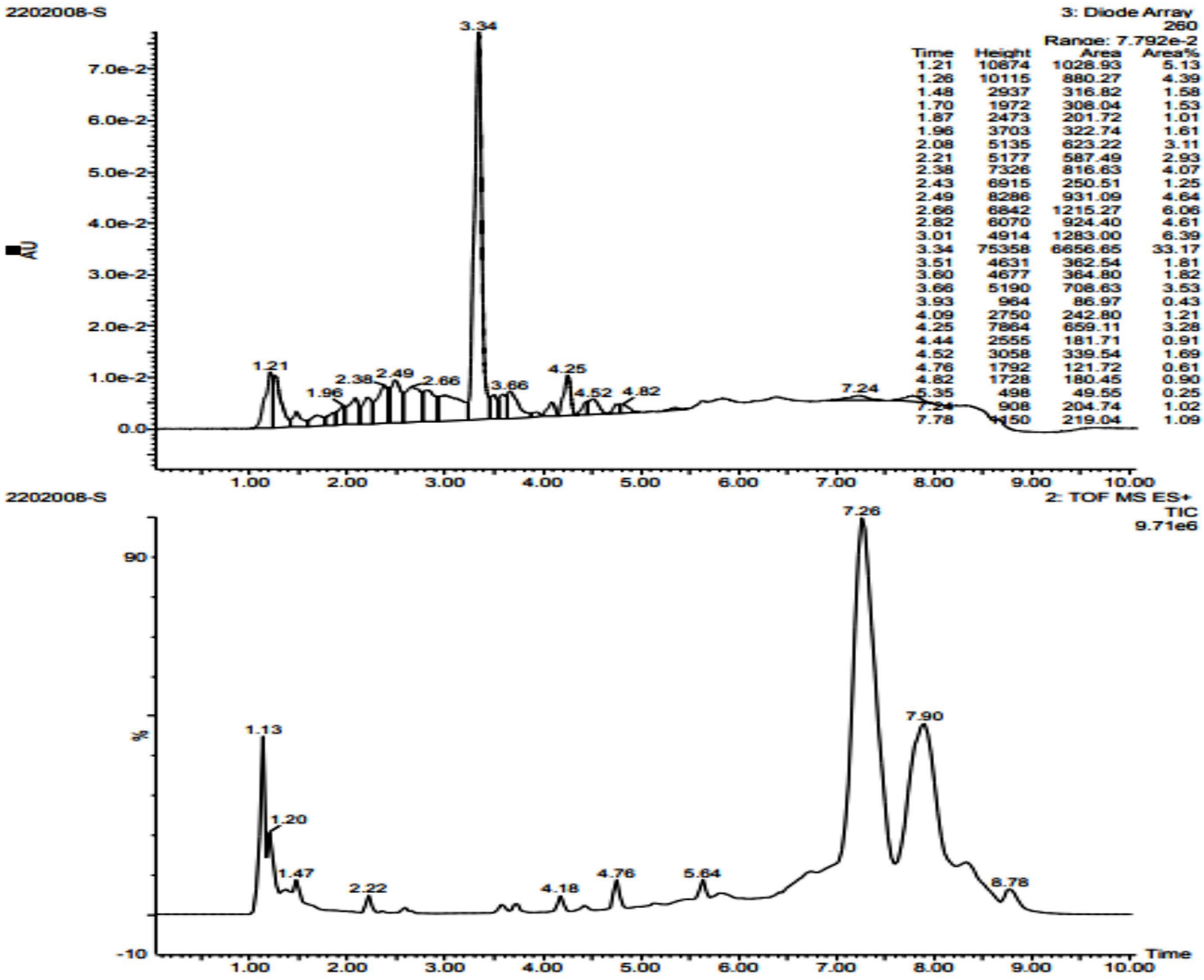


Figure 5: LCMS peaks of JMBG.

attain the free-flowing granules. Methyl and Propyl Parabens were used as preservative due to their effect over a wide range of pH and have a broad spectrum of activity as parabens are the most widely used anti-microbial preservative and are considered to be relatively safer compounds.[38,40] Menthol was used as a flavouring additive and odour enhancer as it has a cooling and refreshing effect. Therefore, the final batch i.e. B16 was selected and further subjected to physicochemical analysis (Table 1).

The pH values of 6.25±0.03 and 5.64±0.005 in 1% and 10% solutions respectively, indicates that the granules are slightly acidic and can be better absorbed in stomach.[41] The ash value of JMBG indicates that final product is free from presence of calcium oxalate and silica by having low acid insoluble ash value and high-water soluble content.[42]

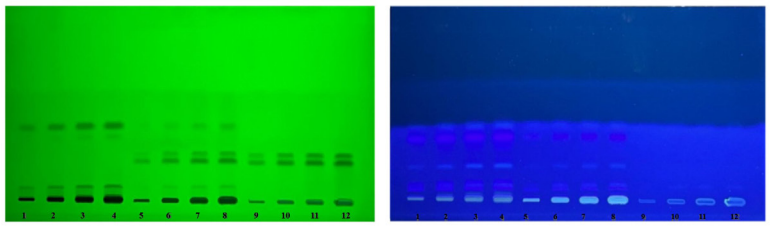
71.83±1.83% and 92.73±0.43 were the highest extractive values that came out to be in water, in successive and non-successive hot Soxhlet extraction methods respectively which concludes that among all the solvents, granules are highly soluble in water. It is obvious as we have used decoction which was extracted in water. Less moisture content of JMBG indicates that modified formulation has higher chances of stability as less value of moisture content suggests that the test drug was of good quality and will prevent bacterial, fungal and yeast growth[43] (Tables 2, 3).

GCMS, LCMS and HPTLC has provided a general insight on the overall phytoconstituents present in the formulation. All the phytoconstituents present have reported pharmacological activities which validates the efficacy of the modified granules to some extent. However further evaluation and establishments will be required (Table 4).

For short term accelerated shelf-life estimation sample was withdrawn at three-month interval and accordingly was evaluated for all the parameters again to check the percentage of degradation due to accelerated conditions, shelf life was calculated as per Grimms formula which states a predictive factor of 3.3 for

Table 4: HPTLC peaks in each track.

Mobile phase	Solvent	Track Name.	Track No.	No. of peaks in each track	
				UV-254 nm	UV-366 nm
M1- Toluene: Ethyl acetate (9.3:0.7)	Aqueous	Pure extract	1, 2, 3, 4	7,7,8,7	2,2,2,2
		Granules (JMBG)	5, 6, 7, 8	6,8,8,7	1,2,2,2
		Excipients	9, 10, 11, 12	3,6,6,8	No peak
	Methanolic	Pure extract	1, 2, 3, 4	6,6,7,7	4,5,7,6
		Granules (JMBG)	5, 6, 7, 8	5,5,10,7	3,4,5,4
		Excipients	9, 10, 11, 12	15,12,12,12	No peaks
M2 - Toluene: Ethyl acetate: formic acid (5:4:1)	Aqueous	Pure extract	1, 2, 3, 4	4,7,6,7	9,10,9,10
		Granules (JMBG)	5, 6, 7, 8	5,4,5,4	4,5,7,8
		Excipients	9, 10, 11, 12	3,4,3,4	No peaks
	Methanolic	Pure extract	1, 2, 3, 4	6,9,7,8	8,11,9,7
		Granules (JMBG)	5, 6, 7, 8	10,11,14,11	7,7,9,8
		Excipients	9, 10, 11, 12	9,10,14,7	5,5,10,1



HPTLC profile in water, mobile phase Toluene: Ethyl acetate: Formic acid (5:4:1) (M2). From 1 to 12: Track 1-4:pure extract, Track 5-8 :granules(JMBG), Track 9-12:excipients in UV 254 nm(Green) and UV 366 nm (Blue)

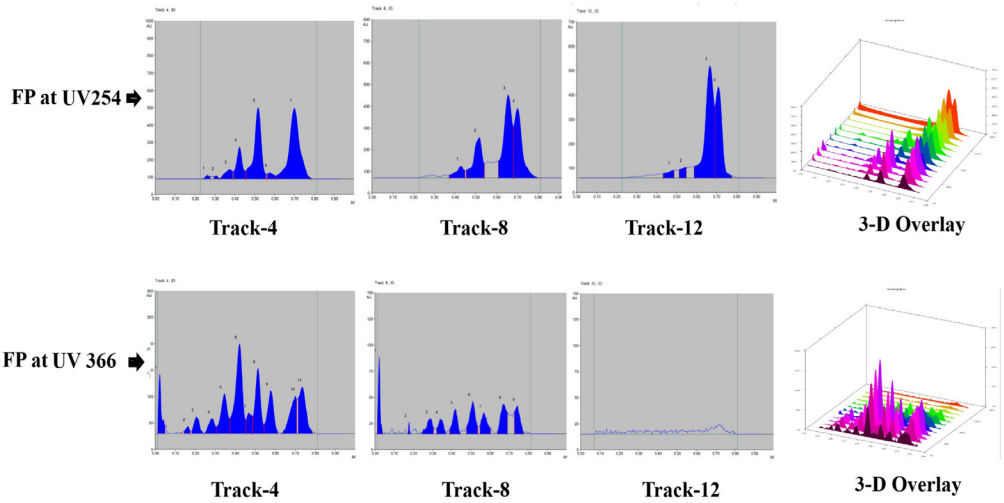


Figure 6: HPTLC Fingerprinting (FP) in Toluene: Ethyl acetate: Formic acid (Solvent-water).

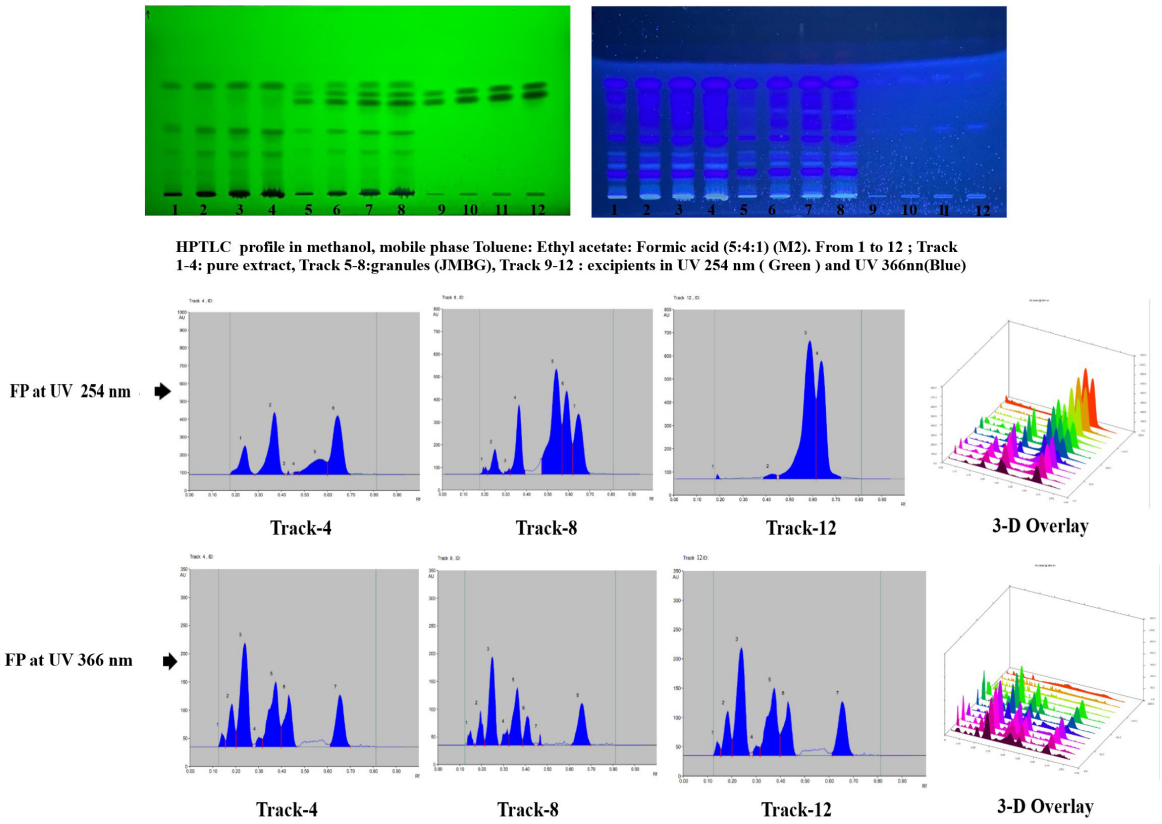


Figure 7: HPTLC Fingerprinting (FP) in Toluene: Ethy acetate: Formic acid (Solvent-Methanol).

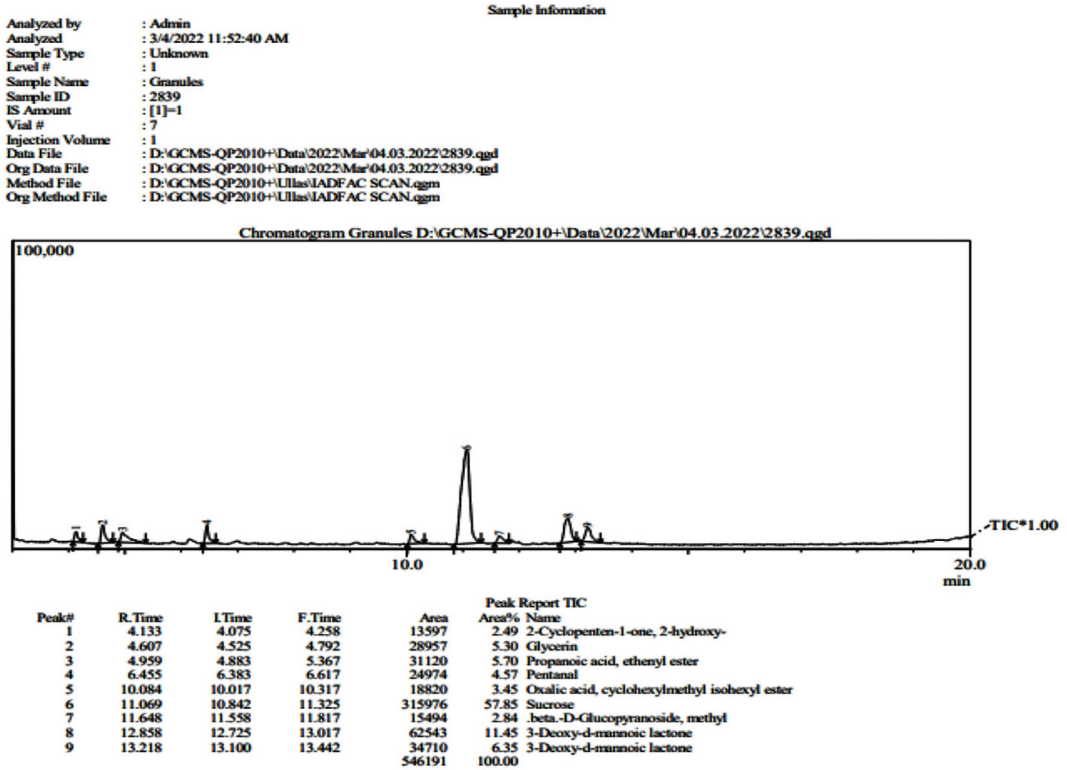


Figure 8: GCMS with NIST - Peak Report TIC at three months (JMBG).

Table 5: Analysis of stability study data (Selected physico-chemical parameters) of JMBG.

Parameter	Day 0 mean %	03 month mean %	Difference %
pH value			
1%	6.25±0.03	5.76±0.016	-7.84
10%	5.64±0.005	5.39±0.014	-4.43
Ash value			
Total ash	1.8±0.11	1.6±0.15	-11.11
Acid insoluble	0.76±0.14	0.63±0.17	-7.10
Water soluble	1.16±0.17	1.06±0.08	-8.62
Total solid content (TSC)			
TSC	51.5±0.98	46.53±0.37	-9.7
Total mucilage content			
TMC	1.01±0.04	0.94±0.005	-6.93
Moisture content			
L.O.D	3.1± 0.05	4.03±0.08	+23.06
T.D	2.76± 0.17%	3.16±0.20	+12.65
Quantitative estimation of phytoconstituents by spectrophotometric method			
Phenols	157.51	150.43	-4.49
Tannins	22.35	22.28	-0.31
Glycosides	2.25	2.22	-1.33
Flavonoids	98.68	94.26	-0.42
Alkaloids	195.5	188.72	-3.46
Quantitative estimation of phytoconstituents by percentage method			
Tannins	0.167 %	0.158 %	-5.3
Flavonoids	0.0078 %	0.0077 %	-1.28
Alkaloids	0.0089 %	0.0087 %	-2.24
Microbial load			
Total bacterial count	1.2×10^2	1.2×10^2	No change
Total fungal count	No growth	No growth	No change
E. coli, *Salmonella*, *S . aureus*, *Pseudomonas*	No growth	No growth	No change

zone IV (India).[44] All the changes at 3rd month in ph value, ash value, total solid content, and total mucilage content were under the permissible specified range as per API. All the quantitatively estimated data of alkaloids, phenols, flavonoids, glycosides and tannins revealed only a slight variation at 3rd month of stability study which indicates that JMB granules has not undergone much degradation as the percentage difference is below 15%. Therefore, the shelf life of JMB granules can be extrapolated as 3.3×3 = 9.9 i.e.10 months, which can be rounded off to one year (Table 5).

The physicochemical and chromatographic tests done on Joshanda (JMB) and the newly formulated Granules (JMBG) generated a standard data for the classical as well as modified formulation.

The quantitative tests of JMBG done by spectrophotometric analysis revealed the quantity of phytoconstituents as Phenols 157.51 µg/mL, Tannins 22.35 µg/mL, Glycosides 2.25 µg/mL, Flavonoids 98.68 µg/mL, and Alkaloids 195.5 µg/mL. There was no significant variation when compared with the values of phytoconstituents found in *Joshanda* (decoction) which resulted in Phenols, Tannins, Glycosides, Flavonoids and Alkaloids as 162.49, 26.29, 2.28, 123.07, 256.29 µg/mL respectively. The highest percentage of difference resulted in Alkaloids which is still below 25% when JMB and JMBG were compared, and the findings suggest that granules may also be therapeutically effective and may correspond to the *Joshanda* in action which can be explored with further scientific studies.

The GCMS scan identified 31 constituent peaks in JMB (Figure 4) and eight peaks in JMBG (Figure 8), with their respective R_f values and area percentage. On comparing with the GCMS report of JMB, it was however concluded that there are reduced number of peaks in JMBG which can be attributed to repeated heat exposure to granules during processing. However, GCMS of JMB generated a standard data which has not been attempted before and can be therefore considered for further research work.

It is a novel research work done on *Joshanda Munzije Balgham* for its modification in granule dosage form. This work can however be taken as the basis to carry out the further research in this direction for further improvisation and exploration of the formulated product, as the aim of the study was to prepare an effective dosage form which can also be feasible, acceptable, accessible, palatable and above all facilitates in patient compliance.

CONCLUSION

JMB was successfully converted into fast dissolving granules JMBG. This can help in improving the shortcomings of traditional *Munzije Balgham Joshanda* to some extent and make it portable, palatable and also increases its shelf life.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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