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Original Article

DESIGN AND EVALUATION OF FAST DISSOLVING GRANULES OF SALBUTAMOL SULFATE

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ABSTRACT

Objective: Appropriateness of administration and patient complaints are important factors in developing dosage forms, especially for children and elderly people. The goal of this research was to develop salbutamol sulfate granules that dissolve quickly to improve patient compliance.

Methods: Five formulas (F1-F5) were prepared by wet granulation methods. Different type of excipients was used in the formulation like banana powder as super disinterring, mannitol, hydroxyl propyl methylcellulose; etc. The formulas were evaluated for flow properties, drug compatibility study by FTIR, drug content, and drug release profile.

Results: The result revealed that the flowability of the five formulas has accepted flow properties; The FTIR studies of the formula F2 showed no drug-excipients interaction. All of the prepared formulas show an acceptable range of drug content, a rapid release of drug of about 95.2% within 10 min. These results indicate good and rapid release properties of salbutamol sulfate from fast dissolving granules.

Conclusion: Salbutamol sulfate was successfully formulated as fast-dissolving granules by using banana powder.

Keywords: Granules, Banana powder, Fast, Salbutamol

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INTRODUCTION

Fast dissolving dosage forms have witnessed a growth in demand over the last decade, and the field has become a rapidly growing area in the pharmaceutical industry. New drug delivery systems (NDDS) are attempting to improve drug molecule safety and efficacy by producing a convenient dosage form for administration to promote patient compliance. "Fast dissolving granules" is one such method. Many patients have difficulty swallowing tablets and hard gelatin capsules, resulting in a high rate of noncompliance and ineffective therapy [1].

The need to give patients with a more traditional means of taking their medication when drinking water is impossible contributed to the idea for quick dissolving/disintegrating granules, as well as in specific instances such as motion sickness, sudden allergy attacks, or coughing. Pediatric and geriatric patients, in particular, encounter these challenges. For pediatric, geriatric, paralytic, nauseated, or non-compliant patients, recent technological advances have provided realistic dosing choices [2].

Scientists have developed Fast-dissolving granules with increased patient compliance and convenience as a result of recent technological advancements. In the absence of additional water, these granules dissolve or disintegrate in the mouth, allowing for convenient delivery of active medicinal substances [3].

The medicine used for the treatment of respiratory diseases is available in traditional tablet and liquid dose forms on the market. From the standpoints of stability and dose measurement, liquid dosage forms have their own set of limitations. Children patients avoid taking tablets, and patient compliance is a problem with such dosage forms. As a result, many do not follow the prescription, resulting in a high rate of noncompliance and unsuccessful treatment [4].

Salbutamol sulfate is a selective, short-acting β2 adrenergic receptor agonist, used in the treatment of asthma and chronic obstructive pulmonary disease (COPD) symptoms like coughing, wheezing, and shortness of breath. Because salbutamol sulfate is water-soluble, preparing it into a fast-dissolving form would cause it to dissolve quickly, resulting in rapid absorption with no lag time [5, 6].

An attempt was made to prepare rapid dissolving granules of a model bronchodilator, salbutamol sulfate, to shorten the lag time and enable a fast onset of action to relieve the immediately acute asthmatic attack.

MATERIALS AND METHODS

Drug salbutamol sulfate was received as a gift sample from samara drug industries, Iraq), Banana powder and mannitol were obtained from Evonik Degussa Ltd., India Pvt. Ltd., USA, hydroxyl-propyl methylcellulose (Gainland chemical company (GCC). U. K.), Saccharine (mg), (Gainland chemical company (GCC). U. K.), polyvinyl pyrolodine (PVP) (Sigma Chemical co. (Aldrich). USA.

Methods

Formulation of fast dissolving granules of salbutamol sulfate

Different formulas as shown in table 1 were prepared; the formulas from F1-F5 were prepared by the wet granulation method.

To guarantee proper distribution of the drug (salbutamol sulfate in the powder combination, all other excipients were weighed properly, passed through filter no 16, and combined according to geometric dilution. After that, enough binder was added to create a wet mass. This bulk was sieved no. 12 to obtain granules, and then the granules put in a hot air oven at 40 °C before being packed in an airtight container [7].

Table 1: Formula used to prepare fast dissolving granules of salbutamol sulfate

Formula no. Ingredient (mg)	F1	F2	F3	F4	F5
Salbutamol	8	8	8	8	8
Banana powder	25	50	100	50	-
Saccharine	10	10	10	10	10
Mannitol	152	122	75	100	100
PVP in alc. 2%	5	5	5	5	5
HPMC in alc. 2%	-	-	-	27	77

Evaluation of salbutamol sulfate granules

The prepared granules were evaluated for the following parameters:

Determination of drug content uniformity

A mount of granules corresponding to 100 mg of salbutamol sulfate accurately measured and mixed with 100 ml of buffer solution (pH 6.8). The solution was clarified; a UV-visible spectrophotometer was used to determine the amount of salbutamol at 276 nm. From the previously prepared slandered calibration cure of salbutamol, the amount of salbutamol sulfate of each sample was determined [8].

Compatibility study

FTIR (Fourier-transform infrared spectroscopy) spectra of salbutamol sulfate alone, excipients, and selected formula by using potassium bromide disc in FTIR spectrometer to ascertain compatibility.

The test was performed at wave number range 4000-400 cm^{-1} at the ambient temperature [9].

Flowability study

The most important parameters for determine the flowability are bulk density (BD), and tapped density (TD). These parameters were measured y using a graduated cylinder (100 ml in size); a suitable amount of granules was weighed and placed, after which the volume of granules was recorded. After that, the measuring cylinder was clicked at 2-second intervals for 2.5 cm height until no change in volume was detected [10].

From equation below, we calculate the BD and TD.

$$BD = \frac{\text{Weight of the granules}}{\text{Volume of the packed granules}}$$

$$TD = \frac{\text{Weight of the granules}}{\text{Tapped volume of the packing granules}}$$

For salbutamol granules, carr's index indicates the compressibility of the powder [11]. Carr's index was determined by the following equation:

$$\text{Carr's index} = \frac{[(TD-BD)*100]}{TD}$$

The output of the above formula was compared with that in table 2.

Table 2: Relationship between powder flowability and % compressibility

Flow description	% Compressibility
Excellent	1-10
Good	11-15
Fair	16-20
Passable	21-25
Poor	26-31
Very poor	32-37

Hausner's ratio of salbutamol granules, calculated according to the following equation. A Hausner ratio of less than 1.25 shows better flow properties than the higher ones. A Hausner 's ratio greater than 1.6 indicates more cohesive powders [12].

$$\text{Hausner's ratio} = \frac{\text{tapped density}}{\text{bulk density}}$$

Angle of repose

Flowability of salbutamol granules was estimated by determination of the angle of repose (θ), the granules are poured freely onto a plane surface, and it forms a cone that has a constant angle between the surface of pile and the horizontal plane. This angle is known as the angle of repose. The angle is calculated by simple geometry from the radius r of the base of the cone and its height h. The inverse tangent of this ratio is the angle of repose [13].

$$\text{Tan } \boldsymbol{\theta} = \frac{H}{0.5*D}$$

Table 3: Properties and correspond the angle of repose

Angle of repose value	Flowing type
<20	Excellent
20-30	Good
30-34	Passable
>40	Very poor

Dissolution study

Dissolution of salbutamol sulfate from different formulas determined by using type II dissolution tester to indicate the release profile of fast dissolving granules, the test was performed in dissolution medium of phosphate buffer solution (pH=6.8), at (37±0.5 °C and 50 rpm). Five milliliters aliquot draw at specific time intervals, and identical volume of medium (5 ml) were replenished to make the dissolution media constant in volume. Filter the drawn samples of solution promptly through a membrane filter paper. The percent of drug released was calculated by checking the absorbance of the solution at 277 nm [14].

Statistical analysis

Standard deviation (SD) was determined for the result of this study as means of three samples (n=3±SD).

RESULTS AND DISCUSSION

The goal of this study was to develop and evaluate fast dissolving granules of Salbutamol sulfate using the wet granulation method.

The results of the flowability test for salbutamol granules were shown in table 4, the bulk density values in the range (0.45 to 0.51) and tapped density between (0.52 to 0.59) respectively. The angle of repose values was a range of 25.5 to 29.98. On the other hand, the car's index result was less than 20 (11.5-13.55). Hausner's ratio values were between (1.13-1.16). The results of the flowability properties of five formulas showed improving to flow properties, improved flow rate and less friction within the bulk. This shows that the mixed mixes have excellent flow properties [15]; also, the improving of flowability properties could be attributed to the manufacturing process, the wet granulation process, in which the granules produced are more spherical and have better flow characteristics than powders [16].

Table 4: Flowability results of salbutamol formulas

Formula code	Bulk density	Tapped density	Angle of repose	Hausner's ratio	Carr's index %	Flow property
F1	0.51±0.12	0.58±0.12	26.88±0.97	1.15±0.02	11.5±0.13	good
F2	0.51±0.08	0.59±0.13	25.5±0.15	1.15±0.76	13.55±0.15	good
F3	0.45±0.09	0.52±0.11	27.72±0.17	1.14±0.11	13.46±0.18	good
F4	0.50±0.08	0.57±0.12	27.9±0.18	1.13±0.98	12.28±0.99	good
F5	0.49±0.15	0.57±0.13	29.98±0.87	1.16±0.67	13.03±0.16	good

*data was expressed as a mean±SD. where n=3.

Compatibility study

Compatibility study was performed to find out the stability or interaction of the drug with excipients. Potassium bromide dispersion was used to measure the spectra in the solid-state. The bands were captured using the Fourier transform infrared (FT-IR) technique. A FT-IR spectrum analysis indicated the presence of identical distinctive peaks. In FTIR studies, the prominent peaks in

the FTIR spectrum of pure drug salbutamol sulfate as shown in fig. 1. it shows an intense band a 1508.38 cm^{-1}, 1616.40 cm^{-1}, and 2982.05 cm^{-1}, 3161.43 cm^{-1} for C=C, N-H,C-H aliphatic, and =CH aromatic group respectively. The result of FTIR spectra indicates that salbutamol was compatible with other excipients indicating no drug-excipients interaction, and all the characteristic IR peaks related to pure drug (like tri-methyl groups, secondary amine group, or phenol groups), were appeared in the IR spectrum of the formulas F2 [17].

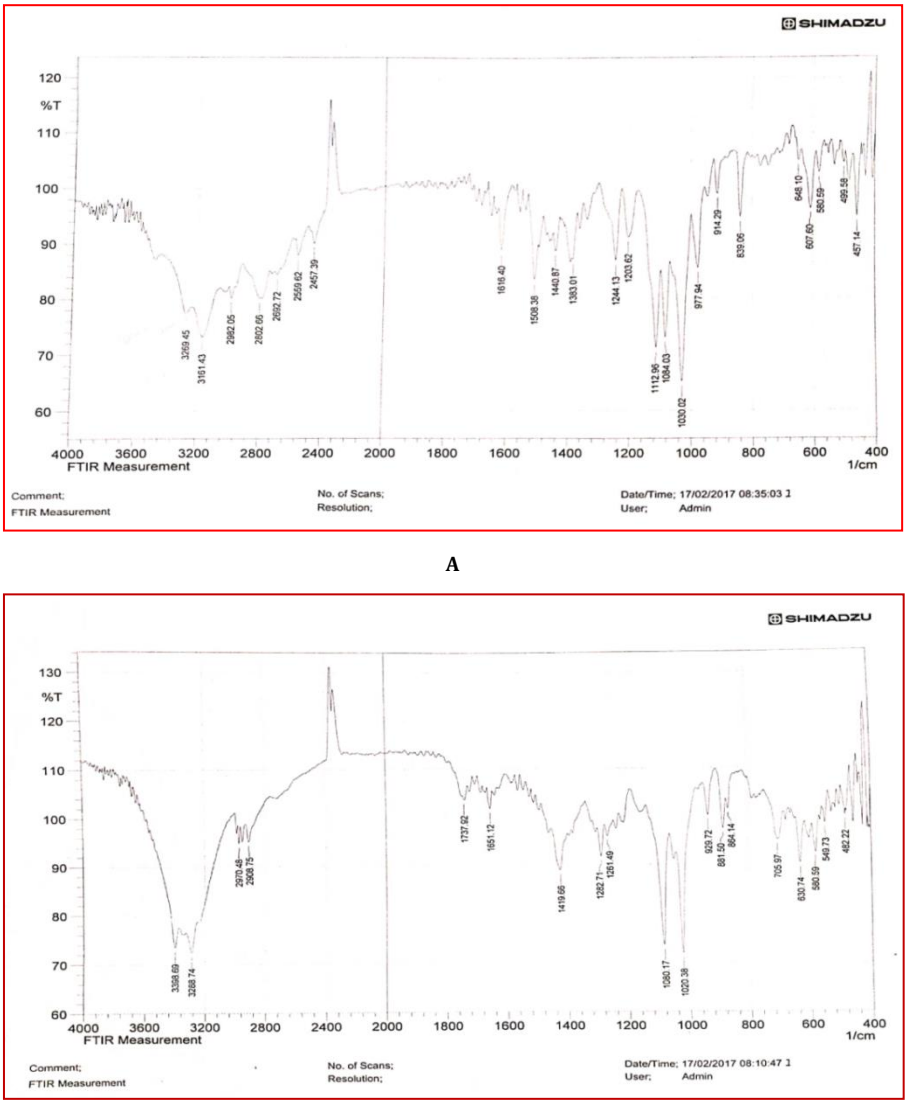

Fig. 1: FTIR spectrum of salbutamol and formula no. 2, where (A) FTIR spectra of pure salbutamol, (B) FTIR spectra of selected formula (F2)

Drug content uniformity

The result of content uniformity was found to be in the range 92.3-97.5.

Table 5 represents the result of drug content. The result of five formulas complies with the pharmacopeia limits [18].

Table 5: Drug content % of the prepared granules of salbutamol sulfate

Formula	Drug content % (w/w)
F1	93.9±0.12
F2	97.5±0.13
F3	95.1±0.11
F4	92.3±0.12
F5	93.2±0.14

*Results expressed as a mean±SD, n=3.

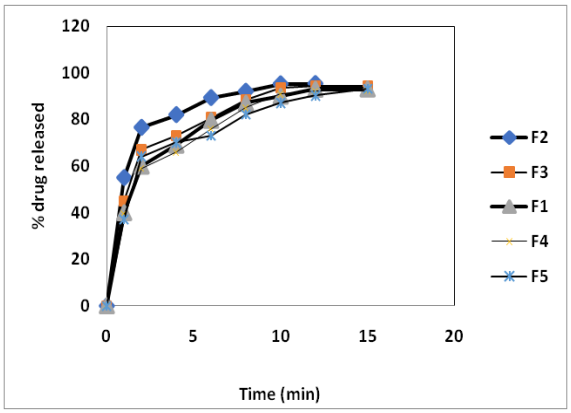

Fig. 2: Percentage of drug release of all five formulations, data is given as a mean of triplicate

Dissolution test

Release profile obtained for the five formulations of prepared granules of salbutamol sulfate are presented in fig. 2. The release profile of salbutamol sulfate granules is 95.3% within 15 min. It was found that all the formulas performed good release within 15 min. using of wet granulation method may be attributed to increase release of drug from prepared formulas by imparting hydrophilic properties to the surface of the granules [19].

F2 was found to be the selected formula due to released 95.2 % within 10 min., which is one of the best release performances among all the five formulas; this occurs due to the role of banana powder which acts as super disintegrating that accelerate the release of drug from granules as reported by other studies [20-24].

CONCLUSION

Salbutamol sulfate was formulated successfully as fast-dissolving granules by the wet granulation method. For this study, it can conclude that fast dissolving granules of salbutamol was successfully formulated by using banana powder. Banana powder, as a natural product with widespread availability, has the potential to be employed as pharmaceutical excipients in a variety of solid dosage forms, particularly in fast-acting formulations. Using banana powder in pharmaceutical formulations will have the extra benefit of being cost-effective and nutritious.

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AUTHORS CONTRIBUTIONS

All authors have contributed equally.

CONFLICT OF INTERESTS

Declared none

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