

EFFECT OF MICROWAVE DRYING IN IMPROVING GRANULE CHARACTERISTICS OF TABLETS

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ABSTRACT

In the ongoing experiment, ibuprofen is used as representative active drug and the granules are formed by using microwave technique and fluid bed drying technique. The granules prepared by microwave technique and fluid bed drying technique are evaluated for the parameters such as, amount of fines, drying time, bulk density, compressibility, angle of repose etc. The study indicated that the granules retained their structure characteristics in comparison with the conventional drying process. The prepared granules are compressed into tablets and evaluated for hardness, friability, disintegration, and dissolution etc. The advantages of microwave drying over the conventional drying technique are enlisted.

Keywords: Ibuprofen tablets, Microwave drying, Fluid bed drying.

INTRODUCTION

Alarming hindrances of classical pharmaceuticals' experiments are longer duration, higher cost, longer reaction time and environmental pollution due to the use of large quantities of solvents/reagents and resources. Drying of granules is the utmost requisite before compression and conventional method of heating inherits certain serious limitations. Since the heating process is very short in microwave procedure, which saves fuel/electricity and chemicals that helps to reduce environment pollution. Following are the few examples of applications of microwave in laboratories like synthesis of drugs, intermediates, chemicals, activation of chromatographic adsorbents, determination of drug loss on drying, enzyme inactivation of food products, hydrolysis of proteins and peptides, saponification of oils, drying of glasswares, sterilization of glass wares and auxiliaries, drying of granules for the preparation of tablets and etc. The wavelengths of microwaves are in a range of about 1 to 10 mm. In microwave spectroscopy, the

source is monochromatic, at a well defined single wavelength which can be rapidly varied. The resolving power is 105 times that of the best infrared grating spectrometer².

The advantages of microwave drying technique are –

1. Microwaves systems are more compact, requiring a smaller equipment space or footprint.
2. Microwaves generate higher power densities, enabling increased production speeds and decreased production costs.
3. The aim of the present study is to standardize the drying process for pharmaceutical granulations by microwave technique and compare the present release of drug obtained by microwave technique with other drying technique.

MATERIAL AND METHOD

Granules were prepared by using ibuprofen as model drug, potato starch as binder as well as disintegrate crosscarmellose and

microcrystalline cellulose as glidant and magnesium stearate was used as lubricant.

PHARMACEUTICAL INFORMATION OF DRUG

Drugs which are coming under the category of NSAIDs e.g. Aspirin, Paracetamol, Nimesulide, Ibuprofen, Aceclofenac, Diclofenac, Meloxicam, Etoricoxib etc. all these drugs have analgesic, antipyretic and anti-inflammatory actions. They act through the mechanism of inhibiting the enzyme cyclooxygenase (COX-1 & COX-2) which is used in the synthesis of prostaglandins, prostacyclin and thromboxane from arachidonic acid.

IBUPROFEN

Category: Anti-inflammatory; analgesic.

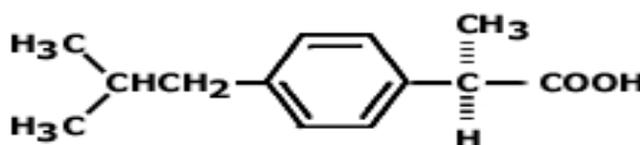
Description: White or almost white, crystalline powder or colourless crystals; odor, slight.

Solubility: Freely soluble in acetone, in chloroform, in ethanol (95%) and in ether; practically insoluble in water. It dissolves in dilute solutions of alkali hydroxides and carbonates.

Chemical Formula: Chemically it is (RS)-2-(4-isobutylphenyl) propionic acid.

Empirical formula of Ibuprofen: C₁₃H₁₈O₂

Molecular Weight: 206.28



and enantiomer

Fig.1: Structure of Ibuprofen

Mechanism of Action: Ibuprofen is an NSAID which is believed to work through inhibition of cyclooxygenase enzyme (COX), thus inhibiting prostaglandin synthesis. There are at least 2 variants of cyclooxygenase (COX-1 and COX-2). Ibuprofen inhibits both COX-1 and COX-2. It appears that its analgesic, antipyretic, and anti-inflammatory activity are achieved principally through COX-2 inhibition; whereas COX-1 inhibition is responsible for its unwanted effects on platelet aggregation and the GI mucosa.

Other ingredients used are Povidone, Alginate, Sodium lauryl Sulphate, Sodium starch glycolate, Magnesium stearate, Cellulose microcrystalline, Potato starch, Colloidal silica,

Procedure for Preparation of Granules by Fluidized Bed Drying (FBD)

Wet granulation technique was used for the preparation of granules⁴. The required quantities of drug and other excipients were weighed and passed through British standard sieve no: 60 to get uniform particle size. The powders are then mixed to get uniform blend. The granulating

medium was added to the powder blend and mixed well until a smooth dough was obtained. The wet granules were passed through sieve no.16 and dried at 60°C for 1 hour in a fluid bed dryer for a batch. The dried granules were passed through sieve no: 16/22 and the granules which passed through sieve no: 16 but retained on sieve no: 22 were selected. The granules obtained through sieve no.22 were considered as fines.

Microwave Granulation Procedure

The required quantities of drug and other excipients were weighed and passed through standard sieve no: 60, to get uniform particle size. The powders were then mixed to get a uniform blend. The granulating medium was added to the powder blend and mixed well until smooth dough was obtained. The wet granules were passed through sieve no: 16 and dried at 840 watts in microwave for different time intervals. After every 15 seconds, the granules were observed for dryness and if not dried, the drying process was continued until the granules were completely dried. After complete drying,

the dried granules were passed through sieve no: 16/22 and the granules which pass through sieve no: 22 were selected. The granules obtained through sieve no: 22 were considered as fines.

EVALUATION OF GRANULES

The granules using both fluid bed and microwave procedure were evaluated for percentage of fines⁵, bulk density⁶, compressibility⁶ and flow properties using angle of repose⁶ and moisture content determinations. Following parameters were evaluated-

Percentage of fines

The granules were passed through standard sieve no: 16/22. The material retained on sieve no: 22 were collected separately and weighed. From this, the percentage of fines was calculated.

$$\text{Carr's consolidation index} = \frac{[(\text{Tapped bulk density} - \text{loose bulk density}) \times 100]}{\text{Tapped bulk density}}$$

Flow properties

A funnel was fixed at a particular height 'h' cm on a burette stand and graph paper was placed below the funnel on table. The sample whose angle of repose is to be determined was poured into the funnel by closing the bottom of the funnel. The bottom was opened and sample was allowed to fall onto the paper. The height of the formed pile was measured and the circumference of the pile was drawn with the pencil on the graph sheet. The radius of the pile was noted as 'r' cm and the angle of repose was calculated as follows:

$$\tan \theta = h/r \text{ or } \theta = \tan^{-1}(h/r)$$

where h=height of the pile, r=radius of pile and θ =angle of repose.

PREPARATION OF TABLETS

The granules were mixed with glidant and lubricant and compressed using a 8-station rotary tablet machine with 10mm standard concave punches. The batch size was 200 tablets. Two batches of tablets were prepared, corresponding to fluid bed drying granulation procedure and other batch corresponding to microwave drying at 840 watt. The prepared tablets were evaluated for weight variation,

Moisture content determinations

Moisture content (loss on drying) of granules before and after drying was determined for both techniques i.e. heat and microwave.

Bulk density

A given quantity of sample was transferred to a measuring cylinder and was tapped mechanically, using a tapping device till a constant volume was obtained, which referred as tapped volume. The bulk density was calculated by

$$\text{Bulk density} = \frac{\text{mass of sample}}{\text{bulk volume}}$$

Compressibility

The compressibility index of the granules was determined by using loose and tapped bulk densities of granules, according to the equation below;

hardness, friability, drug content, and disintegration time and invitro dissolution profile.

In Vitro drug release study

Drug release studies were carried out using USP (XX111) dissolution apparatus following paddle method. Freshly prepared buffer of pH 5.8 (900ml) was placed in the dissolution flask and allowed to attain a temperature of $37 \pm 1^\circ\text{C}$. The tablet was placed at the bottom of the dissolution flask. The paddle was rotated at 50 rpm for 30 minutes. One ml of the sample was withdrawn at different time intervals at 5, 10, 15, 20, 25 and 30 minutes. After each withdrawal, the medium was replaced by equal amount of fresh buffer. The samples were diluted to 10 ml with dissolution medium and used for measurement of absorbance 257nm, in a UV-visible spectrophotometer.

Percentage release of drug = $\frac{\text{Absorbance of sample} \times \text{content of standard} \times \text{Dilution factor}}{\text{Absorbance of standard} \times \text{label claim}}$

RESULTS & DISCUSSION

Evaluation of Granules

One batch of granules corresponding to fluid bed dried wet granulation and other batch corresponding to microwave drying were prepared and evaluated for percentage of fines,

bulk density, compressibility and flow properties using angle of repose. The granule drying time was found to be very less in case of microwave drying. The fluid bed drying method took 60 minutes for complete drying of granules whereas the microwave method took a maximum of 5 minutes at 840 watt. The results of evaluations of granules shown in Table No.1

Evaluation of Tablets

The tablets were evaluated for weight variation, hardness, friability, drug content, disintegration and in Vitro dissolution. The results of evaluations of tablets shown in Table No. 2

Dissolution test

USP dissolution results indicated that the tablets prepared by fluid bed dried granulation and those prepared by microwave granulation at an intensity of 840 watt exhibit good release profiles. The release profile of 98-99.5 % release in 30 minutes time. From the results, it

can be concluded that the batch which was dried at an intensity of 840 watt was ideal batch, and the results were comparable with that of fluid bed dried tablets. Hence, higher intensities can be used for drying of granules in regular classes. The results of in vitro dissolution studies of two batches of tablets were shown in Table No.3 and Figure No.1.

CONCLUSION

This study confirms that microwave drying effectively improve the characteristics of granules in tablets. It can be stated that the tablet granulation can be dried successfully using a microwave oven. By adopting microwave drying technique, tablets can be prepared in less duration of time, at least 10 times less than fluid bed drying procedure. This can save time, energy and cut down the cost of conducting practical classes. Also, use of such technique can reduce environmental pollution.

Table 1: Properties of Ibuprofen granules using Fluid bed and Microwave methods

Physical properties	Microwave dried granules at 840w	Fluid bed dried Granules
Amount of fines (%)	13.61	14.10
Bulk density (g/cc)	0.94±0.006	0.94±0.5
Compressibility (%)	6.15± 0.005	6.02 ± 0.003
Angle of repose (°)	15.99± 0.5	14.94 ±0.42
Drying time (min)	2.8± 0.52	60.2± 0.31
Loss on drying (%)	2.5-3.45	3.0-4.5

All the values are represented as mean ± S.D. n=3

Table 2: Properties of Ibuprofen tablets prepared using fluid bed dried and Microwave dried methods

Evaluation parameters	Microwave dried tablets at 840 w	Fluid bed dried
Average weight (mg)	660± 0.5	607±0.4
Hardness (kg/cm ²)	5.3±0.02	4.56±0.04
Friability (%)	0.109	0.124
Drug content (mg)	508±0.024	506±0.046
Disintegration (sec)	55.02±0.1	44.66±0.4

All the values are represented as mean ± S.D. n=3

Table 3: Cumulative release of drug from the two batches of tablets

Time(min)	Cumulative drug release from Microwave dried tablets at 840 w (%)*	Cumulative drug release from Fluid bed dried tablets (%)*
5	30.15	29.41
10	34.81	31.85
15	49.75	44.59
20	65.93	59.70
25	77.54	74.11
30	99.87	95.54

*Average of three determinations

Table 4: Details of material for core tablet

S. no.	Ingredients	Qty. mg/tab.	Std. Qty.(Kg)
1	Ibuprofen	400.00	125.00
2	Silica colloidal	7.08	2.212
3	Potato starch	87.74	27.42
4	Povidone	11.21	3.503
5	Microcrystalline cellulose	96.85	30.27
6	Alginic acid	10.62	3.320
7	Magnesium stearate	4.72	1.475
8	Sodium lauryl sulphate	2.36	0.737
9	Sodium starch glycolate	14.68	4.587
10	Crosscarmellose	4.72	1.475
	Total weight	640.00	200.00

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