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Formulation and Evaluation of Fast Dissolving Tablets Salmeterol

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Abstract
Recently fast dissolving drug delivery system have started gaining popularity and acceptance as one such example with increased consumer choice, for the reason of rapid disintegration, dissolution, self-administration even without water or chewing. Asthma is a chronic disease of the respiratory system in which the airway occasionally constricts, becomes inflamed, and is lined with excessive amounts of mucus and difficulty in breathing. So the action of drug should be very quickly. The parentrals and aerols have rapid action but its side effect more and patient can become addict to these type of dosage form. So reduce these type of complicance. Fast dissolving tablet of salmeterol play great role in treatment asthma and chronic obstructive pulmonary disease.Salmeterol is a strong bronchodilator .So the fast dissolving tablet of salmeterol so rapid onset of action with the use of superdisintegrant such as crospovidone, primojel. Various techniques are available for prepaing fast dissolving tablet. But the tablets were prepared by direct compression method because in this method tablets are compressed directly from powder mixture of API and suitable excipients. No pretreatment of the powder blend by wet or dry granulation procedure is required.
Key words: fast dissolving tablet, salmeterol, superdisintegrant, direct compression.

Introduction
Fast dissolving tablets disintegrate or dissolve in saliva and are swallowed without the need for water. They are beneficial to swallowing tablets and capsules. Thus difficulty is particularly experienced by pediatric and geriatric patients. Various techniques such as freeze drying, sublimation, spray drying, moulding, mass extrusion and direct compression method have been reported for preparation of mouth dissolving tablets. Several approaches have been employed to formulate fast dissolving tablets involving tablet moulding, freeze-drying, sublimation, spray drying, disintegrants addition-direct compression and use of sugar based excipients. Out of these, disintegrants addition-direct compression is well known technique where disintegrants help to facilitate drug dissolution and consequently improve the bioavailability. Disintegrants that are effective at lower levels and help in rapid disintegration is of great importance in formulations by direct compression. Direct compression, over and above eliminates exposure of heat and moisture during processing and is more economical process. However, the majority of active pharmaceutical ingredients exhibit poor compressibility. Therefore, the addition of directly compressible adjuvant is mandatory. Ideal directly compressible adjuvant must exhibit good flow ability and compatibility. No single adjuvant is likely to possess all the ideal characteristics. For this reason, the current trend in industry is to use multifunctional co-processed excipients. Now a days co-processing is the one of the most widely explored and commercially utilized method for the preparation of directly compressible adjuvant. It can be defined as combining two or more established excipients by an appropriate process. The main aim of co-processing is to achieve a product with added value related to the ratio of its functionality price.

Development of co-processed directly compressible adjuvant starts with the selection of the excipients to be combined, their targeted proportion, selection of preparation method to get optimized product with desired physicochemical parameters and it ends with minimizing avoidance with batch-to-batch variation. Excipients of reasonable price have to be combined with the optimal amount of a functional material in order to obtain integrated product, with superior functionality than thesimple mixture of components. The use of one-body components is justified if it results in a potentiating of the functionalities over that of the dry blend of the functionalities over that of the dry blend of the components prepared by gravity mixture. This synergistic effect should improve the quality

of the tablet equally in all aspects ranging from hardness to dissolution and/ or stability. Co-processing is interesting because the products are physically modified in a special way without altering the chemical structure.Present investigation was aimed to prepared Salmeterolmouth fast dissolving tablets (MFDTs) using co-processed direct compressible vehicles in different ratios employing direct compression technique to improve hardness, reduce disintegration time as well as to achieve satisfactory mouth feel. Salmeterol an important analgesic and antipyretic agent, was chosen for the present work due to its poor compression properties, and therefore requires a binding agent among other excipients to form good quality tablets. Most fast-dissolving delivery system films include substances to mask the taste of the active ingredient. This masked active ingredient is then swallowed by the patient's saliva along with the soluble and insoluble excipients.

Materials and Methods

Materials-

The drug Salmeterol was obtained from as a Gift sample from cipla drugs Ltd. (Mumbai, India). And Sodium saccharine, Wheat starch I.P., Di-calcium phosphate, Crospovidone USP and Aerosil 200 was obtained from CDH New Delhi. Nitric acid, Wheat starch I.P., Magnesium stearate IP and Talc IP was obtained from Institute of pharmacy Bundelkhand University Jhansi.

Methods

Preparation of Tablets

The tablets were prepared by direct compression method using super disintegrant Crospovidone USP and excipients Sodium saccharine, Wheat starch I.P., Di-calcium phosphate, Aerosil 200 , Nitric acid, Wheat starch I.P., Magnesium stearate IP and Talc IP.

Dicalcium phosphate and starch were prepared from co-processed excipients method.

Formulation chart is shown in Table-1

Table.1Formulation chart

S. No	Formulation Code	Salmeterol	Ingredients (mg)	
			Co-Processed Excipient	
			D.C.P	Starch
1.	R1	120	8.89	143.70
2.	R2	120	16.56	140.94
3.	R3	120	24.85	128.75
4.	R4	120	31.75	123.95
5.	R5	120	39.45	110.75
6.	R6	120	47.85	106.45
7.	R7	120	54.5	98.15
8.	R8	120	61.80	90.20

Note: Each formulation (1 tablet) also contained:

Talc	**:**	3 mg
Mag. Stearate	**:**	1.5 mg
Sodium Saccharine	**:**	6 mg
Crosspovidone	**:**	12 mg
Aerosil	**:**	3 mg

Material Properties

1. Angle of Repose:

The angle of repose ofsolid inclusion complexes was determined by the glass funnel method. The accurately weighed quantity of inclusion complexes were passed through the funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touched the apex of the heap of the powder. The powder was allowed to flow through funnel freely onto the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation:

$$\theta = \tan^{-1} h/r$$

Where,

θ = angle of repose
h = height of the cone
r = radius of the cone base

Table.2 Relationship between angle of repose and flowability

Angle of Repose	Flowability
<25	Excellent
25-30	Good
30-40	Acceptable
>40	Very poor

2. Bulk Density

The bulk density was measured by the dividing the mass of a powdered by the bulk volume in cm^3.

$$\rho_b = W/Vb$$

Where,

ρ_b= Bulk Density
W= weight of powder
Vb= volumes of powder

3. Tapped Density (ρ_t):

The tapped density was obtained by dividing the mass of a powder by the tapped volume in cm^3.

$$\rho_t = W/Vt$$

ρ_t=Tapped Density
W= weight of powder
Vt =volume powder

4. Compressibility index

An indirect method of measuring powder flow from bulk densities was developed by Carr. The percentage compressibility of a powder was a direct measure of the potential powder arch or bridge strength and stability. Carr's index of each formulation was calculated according to equation:

$$\text{Carr's index (\% compressibility)} = (\rho_t - \rho_b)/\rho_t \times 100$$

Flow ability of prepared inclusion complex was judged using following correlation:

Table.3 Relationship between % compressibility and flowability

% Compressibility	Flowability
5 – 15	Excellent
12 – 16	Good
18 – 21	Fair to Passable
23 – 35	Poor
33 – 38	Very Poor
> 40	Extremely Poor

5. Hausner's ratio

It provides an indication of the degree of densification which could result from vibration of feed hopper.

Hausner's ratio = Tapped density/ Bulk density

Lower the Hausner's ratio better is the flow property.

Table.4 Correlation between Hausner's ratio and Flow property

Hausner's ratio	Flow property
<1.18	Excellent
1.19-1.25	Good
1.3-1.5	Passable
>1.5	Very poor

Evaluation of Prepared Fast Dissolving Tablets

Evaluation of physical parameters

Uniformity of weight

The uniformity of weight test is run by weighing 20 tablets individually and collectively and calculating the average weight of one tablet, and comparing the individual tablet weight to the average. The tablets meet the Indian Pharmacopoeia (1996) weight uniformity test if not more than two of the individual weights deviate from the average weight by more than the percentage shown in the Table 6.9 and none deviates by more than twice that percentage.

Here, twenty tablets were weighed individually and the average weight was determined. Percentage deviation was calculated and checked for weight variation. The obtained data are shown in Table -5

Table.5 Weight variation tolerances for tablets

Average weight	Percentage deviation
80 mg or less	10
More than 80 mg but less than 250 mg	7.5
250 mg or more	5

Drug Content Uniformity

The test for uniformity of content of single-dose preparations is based on the assay of the individual contents of active substance(s) of a number of single-dose units to determine whether the individual contents are within limits set with reference to the average content of the sample.The preparation complies with the test if each individual content is 85 to 115 per cent of the average content. The preparation fails to comply with the test if more than one individual content is outside these limits or if one individual content is outside the limits of 75 to 125 per cent of the average content. If one individual content is outside the limits of 85 to 115 percent of the average content but within the limits of 75 to 125 percent, repeat the determination using another 20 dosage units. The preparation complies with the test if not more than one of the individual contents of the total sample of 30 dosage units is outside 85 to 115 per cent of the average content and none is outside the limits of 75 to 125 per cent of the average content.

Method:

Five tablets of each formulation were taken and amount of drug present in each tablet was determined. Each tablet was crushed separately and distilled water (about 50 ml) was added to extract the drug. Volume was made up to 100ml with distilled water, and then filtered through Whattman filter paper no. 42, diluted and analyzed in UV spectrophotometer at 234 nm. The obtained data are shown in Table 6.

Hardness

Hardness of tablet is defined as the force applied across the diameter of the tablet in order to break the tablet. The resistance of the tablet to chipping, abrasion or breakage under condition of storage, transportation and handling before usage depends on its hardness. Hardness of the tablet is determined by using hardness tester like Pfizer/ Monsanto.

Hardness test was conducted for three tablets from each batch using Monsanto hardness tester and average values were calculated and are shown in Table-6.

Friability

It is a measure of mechanical strength of tablets. Roche friabilator is used to determine the friability. Preweighed tablets are placed in the friabilator. Friabilator consists of a plastic chamber that revolves at 25 rpm, dropping those tablets at a distance of 6 inches with each revolution. The tablets are rotated in the friabilator for at least 4 min. At the end of test tablets are dusted and reweighed; the loss in the weight of tablet is the measure of friability and is expressed in percentage as:

% Friability = loss in weight / initial weight X 100

The test is run only once unless the results are difficult to interpret or if the weight loss is greater than the targeted value, in which case, the test is repeated twice and the mean of the three tests is determined. A maximum loss of weight (from a single test or from the mean of the three tests) not greater than 1.0 per cent is acceptable for most tablets. If obviously cracked, chipped or broken tablets are present in the sample after tumbling, the sample fails the test. Here, Friability test was performed by using Roche friabilatorand data are shown in Table-6.

Thickness

The crown thickness of individual tablets may be measured with a micrometer. The total crown thickness may be measured with sliding caliper scale. Tablet thickness should be controlled within ±5% variation of standard value.

Thickness was measured using Vernier Calipers. Ten individual tablets from each batch were used and the average thickness was calculated and data are shown in Table -6.

Table -6 Observed physical parameters of Fast dissolving tablets

S. NO	Formulation Code	Drug content	% Weight Variation	Hardness (Kg/cm^2)	Wetting Time (sec)	Disintegration (sec)	Friability (% loss)	Water Absorption Ratio
1	R1	98±0.10	289.68±0.64	3.72±0.10	26±0.34	35±1.30	0.31±0.02	56.30±0.13
2	R2	96±0.70	276.50±0.53	3.54±0.54	15±0.23	21±1.10	0.43±0.05	59.45±0.76
3	R3	93±0.30	304.50±0.75	4.36±0.42	10±0.18	15±0.97	0.47±0.02	64.82±0.35
4	R4	92±0.30	302.91±0.81	4.19±0.24	14±0.26	19±1.03	0.49±0.03	52.78±0.15
5	R5	93±0.29	300.30±0.65	4.75±0.32	14±0.23	18±0.76	0.31±0.01	69.76±0.08
6	R6	95±0.23	300.70±0.85	3.80±0.36	10±0.18	18±1.10	0.48±0.07	41.13±0.11
7	R7	95±0.21	298.50±0.74	3.78±0.34	11±0.17	20±1.19	0.51±0.04	38.13±0.12
8	R8	96±0.83	299.80±0.75	4.78±0.38	12±0.14	33±1.18	0.49±0.06	40.77±0.20

Result and Discussion

Fast dissolving tablets (FDTs) are solid single-unit dosage forms that are placed in mouth, allowed to disperse/dissolve in the saliva without the need of water and provide a quick onset of action. Most fast-dissolving delivery system films must include substances to mask the taste of the active ingredient. This masked active ingredient is then swallowed by the patient's saliva along with the soluble andinsoluble excipients.These are also called melt-in-mouth tablets, repimelts, porous tablets, oro-dispersible, quick dissolving or rapid disintegrating tablets. Oral routes of drug administration have wide acceptance up to 50-60% of total dosage forms. Solid dosage forms are popular because of ease of administration, accurate dosage, self-medication, pain avoidance and most importantly the patient compliance. The most popular solid dosage forms are being tablets and capsules; one important drawback of this dosage forms for some patients, is the difficulty to swallow. Drinking water plays an important role in the swallowing of oral dosage forms. Starch exhibit poor flow and poor compressibility. Hence, it is not widely used as a diluent in direct compression. Starch can be modified by adopting chemical means and used as a diluent in direct compression. The characterization of powder flow was done as per the recently introduced chapter on powder flow in USP. The flow was graded as excellent, good, fair and passable for angle of repose 25-300, 31-350, 36-400 and 41-450 respectively. The angle of repose of starch, acid treated starch and co-processed excipient was 420, 270 and 300 respectively.

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