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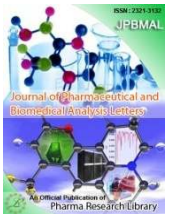

Research Article Open Access

Formulation and Evaluation of Mouth Dissolving Tablets of Betamethasone Using Sublimation Method

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A B S T R A C T

In the present research work mouth dissolving tablets of betamethasone by direct compression method and using rotary tablet compression machine (mfg by lab press) using 6mm punches. To enhance the solubility of drug by sublimation method using sublimating agents like camphor and methanol were developed. After the preformulation studies the formulation blends were subjected to evaluation tests of various precompression and postcompression parameters and all the formulations were found to possess good flow properties. The maximum water absorption ratio was shown by formulation F2, F4 showed 98%. F4 formulation which contains camphor as sublimating agent was shown drug release at 15 min. It was found to be 99.45 ± 0.06.

Keywords: betamethasone, sodium starch glycolate, microcrystalline cellulose.

A R T I C L E I N F O

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1. Introduction

ODT Defines "A solid dosage form containing medicinal substances, which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue". 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 target of these new oral dissolving/disintegrating dosage forms have generally been pediatric, geriatric, bedridden and developmentally disabled patients and also patients with persistent nausea, who are in traveling, or who have little or no access to water are also

good candidates for ODTs. The major advantage of the ODT formulation is that it com- bines the advantages of both liquid and conventional tablet formulations, and also offering advantages over both traditional dosage forms. It provides the convenience of a tablet formulation, and also allowing the ease of swallowing provided by the liquid formulation. ODTs allow the luxury of much more accurate dosing than primary alternate, oral liquid

Advantages

- The more advantage of Mouth dissolving tablets are those when put on tongue disintegrate instantaneously releasing the drug which dissolve or disperses in the saliva.
- The faster the drug into solution, quicker the absorption and onset of clinical effect. The major advantage of the ODT formulation is that it com- bines the advantages of both liquid and conventional tablet formulations, and also offering advantages over both traditional dosage forms.
- Advantageous over liquid medication in terms of administration as well as transportation.
- First pass metabolism is reduced, thus offering improved bioavailability and thus reduced dose and side effects.
- Free of risk of suffocation due to physical obstruction when swallowed, thus offering improved safety.
- Suitable for sustained/controlled release actives

Limitations of mouth dissolving tablets:

- The tablets usually have insufficient mechanical strength. Hence, careful handling is required.
- The tablets may leave unpleasant taste and/or grittiness in mouth if not formulated properly.

Criteria for mouth dissolving tablets:

- Not require water to swallow.
- Be compatible with taste masking.
- Rapid dissolution and absorption of the drug, which will produce quick onset of action.
- First pass metabolism is reduced, thus offering improved bioavailability and thus reduced dose and side effects.

2. Materials and Methods

Aterialsm:

Betamethasone, sodium starch glycolate, microcrystalline cellulose, talc, magnesium stearate.

Methods

Fourier Transforms Infrared Spectroscopy (FT-IR):

FTIR studies were performed on drug, f-melt, optimized formulation using bruker FTIR. The samples were analyzed between wave numbers 4000 and 400 cm^{-1}.

Preparation of Betamethasone Tablets

- Betamethasone tablets are prepared by direct compression method
- Drug, Super disintegrant (Sodium starch glycolate) and different concentrations of sublimating agents (Camphor and Menthol) were weighed and permitted for blending for 5 min.
- The obtained blend was lubricated with magnisium stearate and glidant (Talc) was added and blending was continued for further 5 minutes.
- The resultant mixture was directly compressed into tablets by using 6mm round flat faced punch of rotary tableting machine. Compression force was kept constant for all formulations.

Evaluation of Pre-Compression Parameters:

Angle of repose:

Angle of repose was determined using funnel method. The blend was poured through a funnel that can be raised vertically until a maximum cone height (h) is obtained. Radius of the heap (r) was measured and angle of repose (θ) was calculated using the following formula

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

Bulk density:

Apparent bulk density (ρ_b) was determined by pouring the powder blend into a graduated cylinder. The bulk volume ($V_{b)}$ and weight of the powder (M) were determined.

$$\rho_b = M / V_b$$

Tapped density:

The measuring cylinder containing a known mass of blend (M) was tapped for a fixed time (100 tapping). The minimum volume (V_t) occupied in the cylinder and weight of the blend was measured. The tapped density (ρ_t) was calculated using the following formula.

$$\rho_t = M / V_t$$

Hausner's ratio (h): Hausner's ratio is an indirect index of ease of powder flow. It is calculated by the following formula:

Hausner's ratio (H) = $\rho t/\rho_b$

Where ρt = tapped density

ρ_b = bulk density

% Compressibility index or carr's index:

The simplest way for measurement of free flow of powder is compressibility, an indication of the ease with which a material can be induced to flow is given by compressibility index.

$$\text{Carr's Index} = \rho t - \rho b \ / \rho t \ * 100$$

Where ρ_t = tapped density; $\rho_{b=}$ bulk density

Evaluation of Post Compression Parameters of Betamethasone: Different quality control tests were performed for all the ODT formulations to check whether these have met the specifications given in USP along with other In-vitro tests like wetting time and water absorption ratio. Various tests performed are:

Weight variation test:

20 tablets were randomly selected from each formulation and their individual weights and average weight of all 20 tablets was calculated by weighing on an electronic balance (Shimadzu, AUX 220, Shimadzu Corp, Japan). The Mean ± S.D. were noted.

Thickness:

Randomly 10 tablets were taken from each formulation and their thickness was measured using a digital Vernier caliper (Mitutoyo Corp, Kawasaki, Japan). Average thickness and standard deviation values were calculated. The tablet thickness should be controlled within a ± 5% variation of standard value.

Hardness:
The tablet hardness of different formulations was measured using the monsanto hardness tester. The tester consists of a barrel containing a compressible spring held between two plungers. The lower plunger was placed in contact with the tablet and a zero was taken.

Drug content:
Tablets were randomly selected, weighed and finely powdered and quantity of powder equivalent to one tablet was added to 100 ml of 6.8 pH buffer in a conical flask. A conical flask was then placed on a rotary shaker.

$$\%\text{Friability} = \frac{W\ (\text{initial}) - W\ (\text{Final})}{W\ (\text{initial})} \times 100$$

Where W_1 = Initial weight of 10 tablets.
W_2 = Final weight of 10 tablets

Wetting time:
A piece of tissue paper folded twice was placed in a small petridish containing 6ml of water. A water-soluble dye phenolphthalein was added to the petridish. The dye solution was used to identify the complete wetting of the tablet surface (Abdelbary et al, 2009). A tablet was carefully placed on the surface of tissue paper in the petridish at room temperature. The time required for water to reach the upper surface of the tablets and completely wet them was noted as the wetting time. To check for reproducibility, the measurements were carried out in triplicates (n=3). The wetting time was recorded using a stopwatch.

Water absorption ratio (r):
The weight of the tablet before keeping in the petridish was noted (W_b) using digital balance. The wetted tablet from the petridish was taken and reweighed (W_a) using the same. The Water absorption ratio, R, was determined according to the following equation:

$$R = (W_a - W_b) / W_b * 100$$

W_a= Weight of the tablet after absorption;
W_b= Weight of the tablet before absorption

***In-vitro* dispersion time:**
In vitro dispersion time was determined by placing one tablet in a beaker containing 10 ml of pH 6.8 phosphate buffer at 37±0.5°c and the time required for complete dispersion was determined. To check for reproducibility, the measurements were carried out in triplicates (n=3). The dispersion time was recorded using a stopwatch.

In vitro disintegration time:
The test was carried out on 6 tablets using the disintegration apparatus (Mfg. by Lab India), distilled water at 37°C ± 2°C was used as a disintegration media and the time in second is taken for complete disintegration of the tablet with no palatable mass remaining in the apparatus was measured in seconds.

***In-vitro* dissolution studies:**
Dissolution test was carried out by using USP type II apparatus. The paddle was rotated at 50 rpm. 6.8 pH buffer was used as dissolution medium (900ml) and was maintained at 37 ± 1^{0}C. Samples of 5ml were withdrawn at predetermined intervals (5, 10, 15, 20, 30, 45 and 60), filtered and replaced with 5ml of fresh dissolution medium. The collected samples were suitably diluted with dissolution fluid, where ever necessary and were analyzed for the drug at 242 nm by using ultra violet double beam spectrophotometer. Each dissolution study was performed for three times and mean values were taken.

3. Results and Discussion

Pre formulation studies:
Determination of λ_{max} and preparation of calibration curve of Betamethasone. The regression coefficient was found to be 0.999 which indicates a linearity with an equation of Y=0.056x+0.006. Hence Beer - Lambert's law was obeyed.

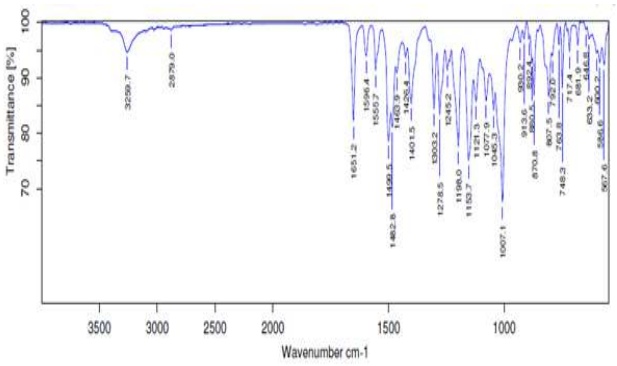

Figure 1: FT-IR Pure Drug

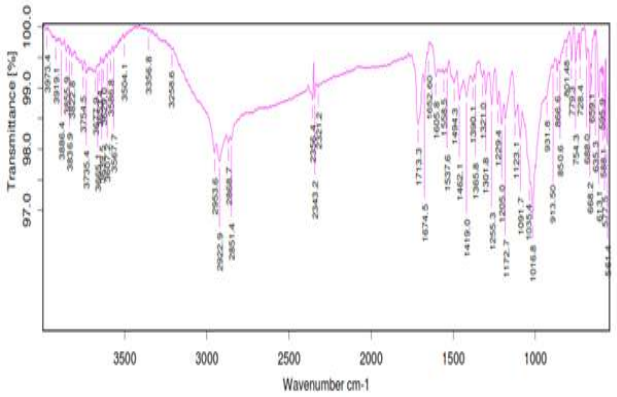

Figure 2: FT- IR Optimized Drug

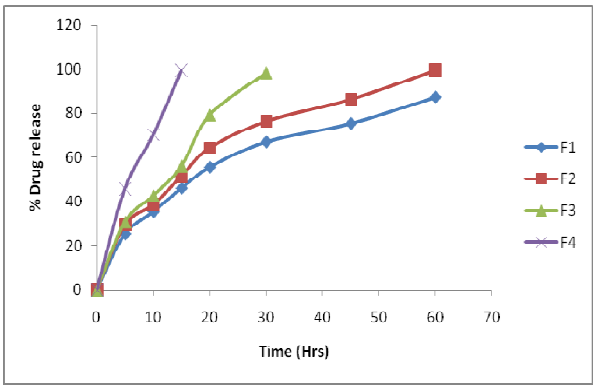

Figure 3: *In-Vitro* dissolution study of Betamethasone MDT tablets containing Camphor

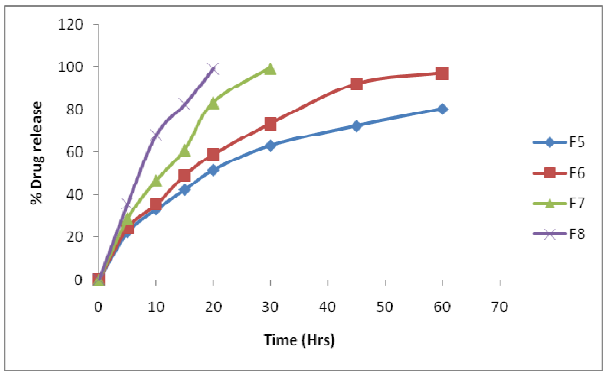

Figure 4: *In-Vitro* dissolution study of Betamethasone MDT tablets contain in Menthol

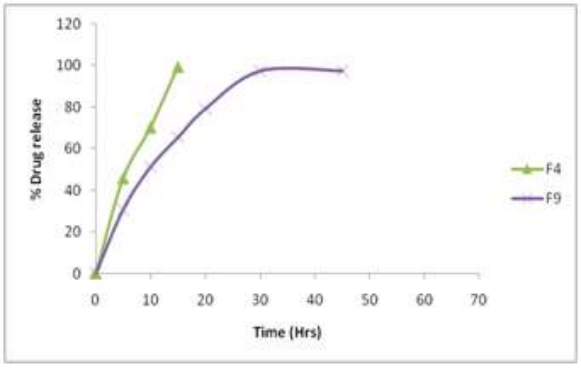

Figure 5: *In-vitro* drug release of F9 formulation containing two sublimating agents camphor and menthol

Table 1: Composition of Betamethasone tablet

Materials (mg)	F1	F2	F3	F4	F5	F6	F8	F8	F9
Drug	5	5	5	5	5	5	5	5	5
Sodium starch glycolate	5	5	5	5	5	5	5	5	5
Camphor	5	10	15	20	-	-	-	-	10
Menthol	-	-	-	-	5	10	15	20	10
Talc	2	2	2	2	2	2	2	2	2
Mg stearate	2	2	2	2	2	2	2	2	2
MCC pH 102	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
Total weight of tablet	100	100	100	100	100	100	100	100	100

Table 2: Evaluation of pre-compression parameters of powder blend

Formulation	Bulk Density* (g/ml)	Tapped density* (g/ml)	Carr's index* (%)	Angle of Repose* (θ)	Hausner's ratio*
F 1	0.51±0.04	0.59 ±0.05	13.55±0.04	27 ±0.05	1.15±0.08
F2	0.48 ±0.05	0.56 ±0.06	14.28±0.06	25 ±0.02	1.16±0.08
F3	0.55 ±0.05	0.63 ±0.06	12.69±0.04	29±0.02	1.14±0.09
F4	0.46±0.08	0.55±0.03	16.36± 0.05	25 ±0.06	1.19±0.07
F5	0.46±0.06	0.53 ±0.02	13.20±0.05	26 ±0.08	1.15±0.07
F6	0.52±0.07	0.60±0.07	15.38 ±0.04	26±0.07	1.15±0.08
F7	0.49 ±0.06	0.56 ±0.07	12.50±0.06	28 ±0.06	1.14±0.06
F8	0.53±0.06	0.63±0.02	15.87±0.03	28±0.06	1.18±0.06
F9	0.48±0.06	0.55±0.02	12.72±0.06	27±0.06	1.14±0.05

Table 3: Evaluation of post compression parameters of Betamethasone Mouth dissolving tablets

Formulation	Weight variation*	Thickness (mm)**	Hardness*** Kg/cm^2	% Friability*	Drug content***
F1	98.4 ±1.35	3.60± 0.05	2.5 ±0.05	0.62±0.08	98.85 ±0.54
F2	102.2 ±1.12	3.65 ±0.04	2.9 ±0.03	0.58±0.06	99.86 ±0.38
F3	99.8 ±1.05	3.73 ±0.06	2.6±0.05	0.65 ±0.06	99.54 ±0.67
F4	100.3 ±1.24	3.79 ±0.06	2.7±0.06	0.62 ±0.05	99.12±0.56
F5	101.6 ±1.31	3.71 ±0.08	2.5±0.08	0.66 ±0.04	98.23±0.36
F6	97.2 ±1.02	3.64 ±0.07	2.9±0.09	0.58 ±0.04	98.64±0.68
F7	99.7±1.46	3.69±0.06	2.8±0.07	0.66±0.05	99.76±0.53
F8	103.8±1.18	3.80±0.05	2.7±0.05	0.60±0.03	97.58±0.67
F9	98.6±1.51	3.66±0.08	2.6±0.07	0.56±0.07	98.36±0.48

Table 4: Evaluation of post compression parameters of Betamethasone Mouth dissolving tablet

Formulation	Disintegrationt time*(sec)	Wetting time* (sec)	*In-vitro* Dispersion Time* (sec)	%water absorption ratio*
F1	29	26	32	96
F2	27	24	29	98
F3	24	21	26	95
F4	18	16	19	98
F5	32	29	35	95
F6	30	27	33	96
F7	26	24	28	95
F8	22	19	24	96
F9	28	26	31	97

Table 5: *In-Vitro* dissolution study of Betamethasone MDT tablets containing Camphor

Time (min)	% DR F1	% DR F2	% DR F3	% DR F4
0	0	0	0	0
5	25.34±0.12	29.4±0.84	30.8±0.73	45.75±0.67
10	35.42±0.29	38.6±0.67	42.72±0.61	70.24±0.12
15	46.15±0.08	51.6±0.19	56.16±0.44	99.45±0.06
20	55.64±0.34	64.3±0.36	79.4±0.38	
30	67.12±0.72	76.4±0.41	98.5±0.52	
45	75.48±0.36	86.4±0.27		
60	87.43±0.14	99.56±0.22		

Table 6: *In-Vitro* dissolution study of Betamethasone MDT tablets contain in Menthol

Time (min)	% DR F5	% DR F6	% DR F7	% DR F8
0	0	0	0	0
5	22.37±0.31	24.46±0.13	28.8±0.69	35.72±0.17
10	33.18±0.56	35.39±0.08	46.72±0.37	68.16±0.38
15	42.39±0.12	49.22±0.15	61.16±0.18	82.56±0.61
20	51.68±0.43	58.91±0.27	83.43±0.30	99.26± 0.43
30	63.17±0.38	73.54±0.06	99.51±0.09	
45	72.49±0.56	92.14±0.38		
60	80.48±0.43	97.24±0.41		

Table 7: *In- vitro* drug release of F9 formulation containing two sublimating agents camphor and menthol

Time (min)	% DR F
0	0
5	30.78±0.33
10	51.29±0.19
15	65.42±0.28
20	79.19±0.77
30	97.38± 0.43
45	97.38± 0.43

4. Conclusion

Mouth dissolving tablets of Betamethasone formulated using sublimating agents along with super disintegrant sodium starch glycolate study concluded that all the formulations were shown good pre compression and post compression parameters. Among all formulations F4 formulation shown optimum drug release which was enclosed with camphor as sublimating agent.

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