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Formulation Development & Evaluation of caffeine tablets (200mg) by Direct Compression

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Abstract: Direct compression is a simplest, time saving and economical way of tablets' manufacturing. It is just a mixing and compression of dry blend of powder. The aim of study is to prepare caffeine tablets (200 mg) by direct compression. Three formulations F1, F2 and F3were prepared, containing different combinations of Avicel and DiTab, keeping the amount of drug and magnesium stearate constant. Micromeritic properties of blend and powders were determined, including carr's index, hausner ratio, angle of repose and particle distribution analysis. Different compendial and non- compendial tests were performed to assess the quality of directly compressible tablets. F2was an optimized product as it is superior in terms of better weight variation, hardness, percent release (99.02%) and assay (100.02%).On the basis of results it is concluded that the caffeine tablets could be satisfactorily produced by direct compression.

Keywords: Caffeine, Tablets, Direct Compression, Stability testing, Formulation Development.

INTRODUCTION:

There are different methods of tablet manufacture with choice depending on the dose and the drug's physical properties such as compressibility and flow (1). Direct compression is a major formulation process in pharmaceutical technology. It is a process by which tablets are compresses directly from mixtures of the drug and excipients without any preliminary treatment (2). The formulation of direct compression is simple including an active pharmaceutical ingredient (API), a diluent, a disintegrant and a lubricant (3). A survey was conducted in 1992 regarding the preference of manufacturing technique by pharmaceutical industries; about 41.5% were in favor of direct compression (4). Pharmaceutical industries are now focusing towards direct compression since it is more economic (consequent reduction in appliance and handling costs), less time consuming, least chances of cross contamination (5) and straight forward in terms of good manufacturing practice requirements than are wet granulation and dry compaction (6).

Excipients with optimal functionality are needed to ensure smooth tablet production on modern machines (7). The majority of excipients that are currently available failed to live up o functionality requirements, thus creating the opportunity for the development of new high-functionality excipients (8). Typical examples of direct compaction filler-binders are the free-flowing lactose (spray dried or agglomerated), calcium phosphates, compressible starch, microcrystalline cellulose, mannitol, sorbitol and sucrose (compressible sugar). Each of these is available in different physical forms having their special advantages in the direct compaction process (9).

Caffeine is a bitter, white crystalline alkaloid structurally identified as 1,3,7-trimethylxanthine. It occurs naturally in coffee beans, tea leaves, kola nuts and cocao beans (10). Ingested caffeine is rapidly absorbed and extensively metabolized to paraxanthine derivatives(11). It is most popular psychoactive consumed substance in the world to obtain mild CNS stimulant effects. Blockade of methylxanthine-sensitive adenosine receptors is the currently accepted mechanism (12). Practioners should know the contribution of dietary caffeine since the toxic effects of caffeine are extensions of their pharmacological effects. The most serious caffeine-related CNS effects include seizures and delirium. Other symptoms affecting the cardiovascular system range from moderate increases in heart rate to more severe cardiac arrhythmias(13).

Material and Method:

Material:

Caffeine anhydrous, (gifted by Herbion pharmaceuticals), DitAb (FMC Corporation), Microcrystalline cellulose (PH102) and magnesium stearate (FMC Corporation) were the chosen ingredients. Formulation is given in table 1. All ingredients were passed through sieve 60 and mixed using local fruit blender for one minute. Single punch machine (KORSCH Erweka, Frankfurt Germany) was used for direct compression having caplet shaped punches of size 9x8mm.

Optimization:

Three different formulations of caffeine tablets F1, F2 and F3 were prepared by changing the amount of Avicel PH 102 and DiTab (binders/filler) keeping magnesium stearate and the drug constant. The target weight in all three formulations is 375 mg ±18.75.

Table 1: Formulation of caffeine Tablets

Components	F1 (mg/tablet)	F2 (mg/tablet)	F3 (mg/tablet)
Caffeine (API)	200	200	200
MC (PH102)	85	128	42
DiTab	85	42	128
Magnesium stearate	5	5	5
Total (mg)	**375**	**375**	**375**

Micromeritic Properties of Blend:

Particle Size Distribution Analysis:

Each ingredient of the dry blend; Caffeine, Avicel PH102, DiTab and magnesium stearate were subjected to particle size analysis using the ROTAP sieve shaker. Sieves were arranged in the order of increasing mesh numbers with a collecting pan at the bottom. 50g of the sample was placed on the top most mesh, fitted into the ROTAP shaker and run for 5 minutes. The amount of powder retained on each of the sieves was noted to obtain the Particle size distribution.

Flowability Indices

Carr's Index and Haussner's ratio were determined through bulk and tapped densities using following formula is given below.

$$\textit{Carr's Index} = \frac{\rho_{Tapped} - \rho_{Bulk}}{\rho_{Tapped}} \times 100$$

$$\textit{Haussner's Ratio} = \frac{\rho_{Tapped}}{\rho_{Bulk}}$$

Carr's index greater than 25% indicates poor flowability, while lesser than 15% shows excellent Flowability and Haussner's ratio >1.25 corresponds to poor flow properties (USP).

Angle of Repose:

Each ingredient of the dry blend; Caffeine, Avicel PH102, DiTab and magnesium stearate were poured into a funnel and a conical heap was

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formed on a flat surface. The height and diameter of the heap was measured and the Angle of repose was calculated as:

$$\tan \theta = 2h/D$$

Blend Homogeneity

Blend homogeneity was performed at three different time intervals (1 min, 3 min and 5 min). The suitable blending time is that where least % RSD is achieved.

Evaluation of Compressed Tablets:

Weight Variation: The variation of the weight is a valid indication of the corresponding variation on the drug content. The average tablet weight was determined by weighing 20 randomly selected tablets using an electronic balance (Mettler Toledo B204-S, Germany).

Hardness Testing: To test for the hardness of the tablets, 20 tablets were randomly selected and evaluated using Hardness (Varian VK 200 tablet hardness tester Beenchsaver Series).The average hardness (Kg) and standard deviation were calculated for optimized batch F2.

Friability Testing: The tablets' surface resistance to abrasion was evaluated using a friabillator. Tablets were de-dusted before weighing and then placed in a friabillator (Vankel Friabilator) and rotated at 25 rpm/min for 4 minutes. The tablets were removed, de-dusted, re-weighed. Percent friability was calculated using formula

$$\%\,friability = \frac{(initial\ weight - final\ weight)}{Initial\ weight} \times 100$$

Visual observation was also used to scan through the tablets' surface for any sign of apparent defects such as cracks.

Disintegration: Six tablets were randomly selected and placed in each tube of disintegrating assembly (Varian Model VR100 35-1200) containing distilled water as medium.

Dissolution: Six tablets were added in the dissolution apparatus (Vankel VK 700) containing the dissolution media. 900 ml of water was used as the media to mimic GI track in vivo. The dissolution machine was set on at a speed of 50 rpm and the sample in the dissolution was drawn at 60 minutes. The drawn sample was analyzed using the UV-spectrophotometer at a wavelength of 272 nm (14).

Assay: The assay was performed using liquid chromatography. The mobile phase and other specifications were taken from an official monograph given in USP 2009.

Results

Table 2: Flowability Indices and Particle Size of the bulk powders and Dry Blend

Component	Angle of Repose (°) mean ± SD)	Carr's Index	Haussner's Ratio	Particle Size (µm)
Caffeine	27.65 ± 5.29	40.02 %	1.6	172.11
Avicel PH102	36.15 ± 3.29	23.0 %	1.42	117.38
DiTab	26.57 ± 2.25	29.0 %	1.16	184.30
Magnesium Stearate	26.79± 0.49	32.6 %	1.48	44.02
DC BLEND	17.92 ± 2.6	21.5 %	1.15	201.21

Table 3: Evaluation of physic-chemical properties of tablets

Tablet properties	Results
Weight variation (mg)	375.05±3.53
Hardness (Kg)	7.57±0.684
Percent friability	0.04
Disintegration time (min)	8 to 10
Average Percent Dissolution	99.2
Average Percent Assay	100.4

Figure 1: weight variation of Tablets (F2)

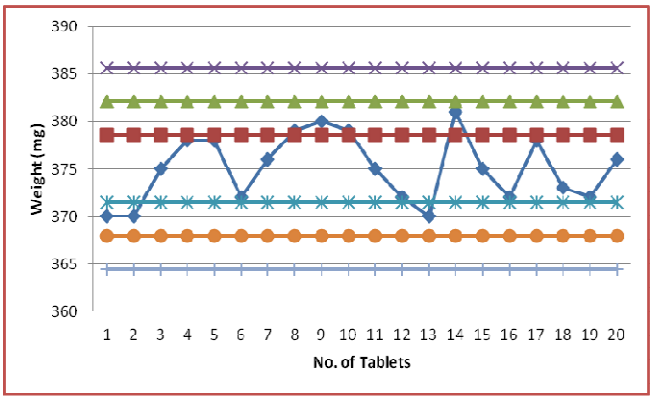
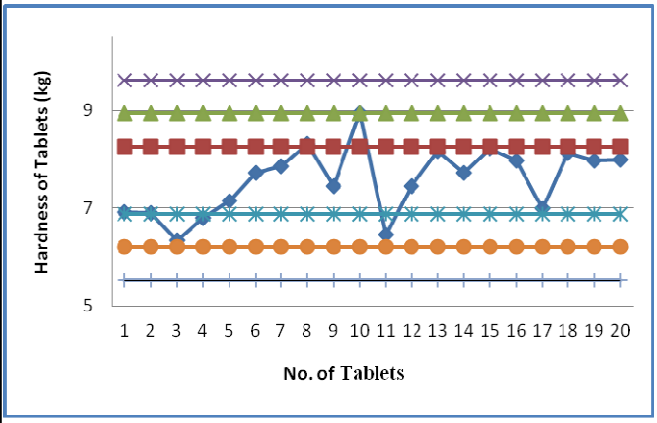


Figure 2: Hardness (Kg) of Tablets (F2)



Discussion:

Solid dosage forms like tablets and capsules are the most popular and preferred drug delivery systems because they have high patient compliance, relatively easy to produce, easy to market, accurate dosing, good physical and chemical stability (15, 16).In this study three different formulations (F1, F2 and F3) were prepared by changing the amounts of filler/binder (Avicel PH 102, DiTab) while the drug and magnesium stearate was kept constant. The formulations were given in table 1 & the powder properties are shown in table 2. Out of three formulations F2 was an optimized formulation. The batches were mixed at different timings. The least % RSD was found to be at 1 minute. Mixing time is especially very critical when batch size is small. Since over mixing may lead to segregation of the blend. All the physico-chemical parameters were within the acceptable limits (Table 3). Compressed tablets may be characterized or described by a number of specifications. These include the diameter, shape, thickness, weight variation, hardness, disintegration time, and dissolution characteristics (17, 18).

The combination of Avicel and Ditab was perfect in F2 and provide optimum hardness to tablets. The hardness of 20 randomly selected tablets with 3 upper control limits and 3 lower control limits is illustrated in figure 2. The target weight of the formulation was 375 mg; F2 showed least weight variation among 20 randomly selected tablet units. Figure 1 shows the weight of 20 tablets with three upper and lower control limits. It is clearly shown in graph that no tablet crossed 2nd and 3rd upper and lower limit of weight. One of the most common problems associated with direct compression is the lack of uniform flow. But the addition of magnesium stearate increases the uniform flow of powder blend from hopper to die. It is well documented that lubricant is a formulative excipient that reduces the friction between the die and punches as well as some times acts as anti- adherent also (19-22). Lubricant also has profound influence on disintegration time, hardness and drug dissolution (23, 24).

Dissolution is an in-vitro tool to determine an in vivo bioavailability. Dissolution was performed according to an official monograph given in USP, 2009. Tablets showed excellent percent dissolution within 60 minutes. The assay which was performed using liquid chromatography was also within the official limit. The results of weight variation, dissolution, and assay all were is an excellent range, showing none of the problem like segregation, loss of content uniformity and others.

Hence caffeine tablets manufactured by direct compression are excellent in terms of tablet attributes.

CONCLUSION:

Caffeine tablets are successfully prepared by direct compression technique. All compendia and non-compendial tests were within the acceptable limits. Therefore it is concluded that direct compression is simplest, easiest and economical means of tablets' manufacturing.

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