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Evaluation and Comparison of Highly Soluble Sodium Stearyl Fumarate with Other Lubricants In Vitro

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ABSTRACT

Lubricants are the essential components of all solid dosage forms. Sodium stearyl fumarate is sparingly soluble in water. An attempt has been made to improve solubility of sodium stearyl fumarate to become it highly soluble. Sodium stearyl fumarate was compared with other conventional lubricants to check the impact of lubricants on flow properties, hardness, and disintegration and dissolution characteristics. Different concentrations of lubricants were used to prepare uncoated tablets and evaluated for its activity. All the tablets prepared with sodium stearyl fumarate were found to be better in terms of variations in hardness, disintegration and dissolution property. Hence, sodium stearyl fumarate was a super lubricant in tablet dosage form.

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Introduction:

Tablet lubricants are essential components of all tablet formulations, since they prevent sticking of the tablets in the dies. Without tablet lubricants, tablets can't be prepared. A lubricant may be defined as a suitable material, a small amount of which interposed between two rubbings surfaces will reduce friction arising at the interface. [1]

Lubricants have a number of functions in tablet manufacture.

a) They reduce interparticle friction.
b) It facilitates the ejection of the tablet from the die cavity.
c) It may improve the rate of flow of the tablet granules. [2, 6]

Lubricants are pharmaceutical excipients that improve the fluidity, filling properties, adhesiveness and plasticity of powders and are indispensable for improving the quality and manufacturing efficiency of solid preparations. Insufficient fluidity of the bulk powder in the tabletting process causes problems such as an increased in the variability of the tablet weight, impairment of content uniformity, and deterioration of the product quality. Also, inadequate plasticity due to friction and adhesion among powder particles or between the particles and the punch and die directly leads to trouble in the manufacturing process and deterioration for avoiding for such trouble. Hence, ensure appropriate quality parameters for finished products, reflective of uniform accuracy, safety and therapeutic efficacy. [3, 4]

Ideal Properties of Lubricant:

a) It should be capable of reducing friction effectively in small quantities with no adverse effect upon the formulations.
b) It should be inert and cosmetically acceptable with respect to other dosage form ingredients.
c) It should be white and odourless but water solubility may also be an essential requirement.
d) It should be unaffected by changes in process variables, consistent from batch to batch
e) It should be readily available and cheap.[1, 5,7]

Advantages of sodium stearyl fumarate in comparison with magnesium stearate and talc

a) Sodium stearyl fumarate is an inert, hydrophilic lubricant for tablets.
b) Superior tablet hardness at equivalent compression force.
c) Lower ejection force at equivalent compression force.
d) Less impact on disintegration times.
e) Performance varies with blending time or lubricant level.
f) Solves incompatibilities with Magnesium stearate
g) Semi soluble so lower residue when in solution or effervescent preparations.
h) Especially effective in oral dispersible tablets (ODT).
i) Usage level of 0.25 to 3 % w/w concentration.
K) Excellent substitute for Magnesium stearate and Talc.[9,10]

Uses of Sodium stearyl fumarate [8, 9]

a) To avoid metallic taste of magnesium stearate
b) In combination with organic salts.
c) For APIs with carbonyl- carboxyl groups.
d) For APIs with sulfo groups.
e) For high speed direct compression.

OBJECTIVES:

Magnesium stearate and Talc are the hydrophobic lubricants which have tendency to coat the individual particles. Hence, these lubricants are generally associated with hardness variability, poor tablet disintegration and drug dissolution. The purpose of this study was to evaluate the ability of sodium stearyl fumarate to reduce friction and adhesion as well as its effect on tablet strength, disintegration and dissolution.

MATERIALS AND METHODS

Diclofenac sodium was gifted by Blessings Pharmaceuticals, Nagpur. Micro crystalline cellulose was supplied by NB Entrepreneurs, Nagpur. Sodium starch glycollate was purchased from Loba chemicals Mumbai. Highly soluble Sodium stearyl fumarate, Magnesium stearate, Talc was provided by Nitika Chemicals, Nagpur. All other chemicals used were of analytical reagent grade.

Formulations of various batches of diclofenac sodium tablets:

Ingredients mentioned in the following table no. 1, were used for the formulations of various batches of diclofenac sodium tablets by direct compression method. The ingredients were weighted, sifted through sieve No. 44 were mixed in geometrical order and compressed by 6 mm punch to get tablets of 100 mg weight using 10 station single rotary Rimek mini press tablet compression machine. Formula for diclofenac sodium was given in table as follows.

TABLE 1: FORMULA FOR DICLOFENAC SODIUM TABLETS

Batch code	Diclofenac sodium	Micro crystalline cellulose	Sodium starch glycollate	Sodium stearyl fumarate	Magnesium stearate	Talc
S1	50	47.5	2	0.5		
S2	50	47	2	1		
S3	50	46.5	2	1.5		
S4	50	46	2	2		
S5	50	45.5	2	2.5		
M1	50	47.5	2		0.5	
M2	50	47	2		1	
M3	50	46.5	2		1.5	
M4	50	46	2		2	
M5	50	45.5	2		2.5	
T1	50	47.5	2			0.5
T2	50	47	2			1
T3	50	46.5	2			1.5
T4	50	46	2			2
T5	50	45.5	2			2.5

For tablets prepared by direct compression method, specified quantities of Diclofenac sodium, Micro crystalline cellulose, Sodium starch glycollate, highly soluble Sodium stearyl fumarate, Magnesium stearate, Talc were weighed accurately and passed through 60 mesh screens. All the materials were transferred to a mortar and triturated till it was uniform. The resulting powder blends was evaluated for bulk density, tapped density, Carr's index, angle of repose and Hausener's ratio mentioned in table no. 2, 3, 4 respectively and compressed by 6 mm punch to get tablets of 100 mg weight using 10 station single rotary Rimek mini press tablet compression machine.

TABLE 2: FLOW PROPERTY OF POWDER WITH SODIUM STEARYL FUMARATE

Batch. No	Bulk density	Tapped density	Compressibility index	Hausner's ratio	Angle of repose (θ)
S1	0.50	0.55	9.14	1.10	17
S2	0.47	0.53	11.32	1.13	20
S3	0.42	0.51	15.69	1.19	23
S4	0.37	0.48	22.92	1.30	27
S5	0.33	0.44	25	1.33	31

TABLE 3: FLOW PROPERTY OF POWDER WITH MAGNESIUM STEARATE

Batch. No	Bulk density	Tapped density	Compressibility index	Hausner's ratio	Angle of repose (θ)
M1	0.49	0.54	10.91	1.12	19
M2	0.45	0.52	13.46	1.16	22
M3	0.41	0.50	18	1.22	25
M4	0.35	0.47	25.53	1.34	30
M5	0.30	0.42	28.57	1.40	34

TABLE 4: FLOW PROPERTY OF POWDER WITH TALC

Batch. No	Bulk density	Tapped density	Compressibility index	Hausner's ratio	Angle of repose (θ)
T1	0.49	0.55	11.65	1.14	18
T2	0.45	0.53	15.09	1.18	21.5
T3	0.40	0.50	20	1.25	26
T4	0.34	0.46	26.09	1.35	31
T5	0.29	0.41	29.27	1.41	35

Evaluation of Tablets

Compressed tablets were examined physically for the shape of the tablet. The thickness of tablet was determined with the help of vernier calipers. The thickness variation was allowed in the range of + 5% of the size of the tablet. With a tablet designed to contain a specific amount of drug in a specific amount of tablet formula, the weight of the tablet being made is routinely measured to help ensure that a tablet contains the proper amount of drug. The USP weight variation test was run by weighing 20 tablets individually, calculating the average weight, and comparing the individual tablet weights to the average. The tablets meet the USP test if no more than 2 tablets are outside the percentage limit.

The tablet was triturated to form a fine powder and transferred to a 100 ml volumetric flask and dissolved in phosphate buffer pH 7.2 and was made up to the volume to get stock solution. 1ml of this stock solution was taken in a 100ml volumetric flask and diluted with phosphate buffer pH 7.2 and made up to the volume. The absorbance of this solution was measured at 276nm using UV spectrophotometer. The drug content was estimated from the absorbance obtained.

Friability was determined using a Roche model friabilator and hardness was determined using a Monsanto hardness tester. The in vitro disintegration time was determined by using disintegration test apparatus.

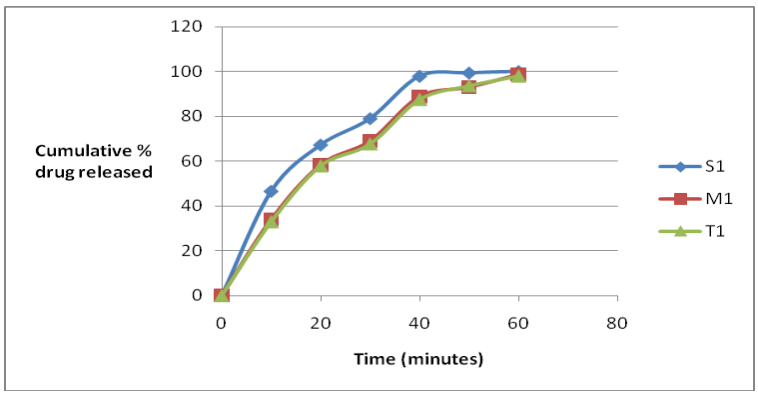
TABLE 5: PHYSICAL PROPERTIES OF TABLETS

Batch code	Thickness (mm)	Weight uniformity (mg)	Hardness (kg/cm^2)	Friability (%)	Disintegration time (minutes)	Content uniformity (%)
S1	2.09	101±0.015	6.3	0.35	3.09	98.23
S2	2.14	99±0.021	5.4	0.44	3.30	98.76
S3	2.03	103±0.023	4.8	0.50	4.10	97.91
S4	2.07	101±0.025	4.2	0.55	4.49	99.39
S5	2.05	100±0.017	3.5	0.60	5.31	98.54
M1	2.09	103±0.019	6.5	0.33	3.54	98.76
M2	2.07	100±0.021	5.2	0.46	4.30	99.31
M3	2.10	99±0.023	4.4	0.53	5.17	101.30
M4	2.05	102±0.025	3.6	0.60	6.20	98.70
M5	2.11	101±0.027	2.8	0.67	7.39	97.48
T1	2.05	101±0.023	6.1	0.37	3.48	98.23
T2	2.06	100±0.020	5	0.48	4.36	98.67
T3	2.10	103±0.024	4.2	0.55	5.26	99.51
T4	2.03	101±0.019	3.4	0.62	6.32	98.13
T5	2.07	100±0.016	2.6	0.69	7.50	99.27

All values are in SD ± n =3

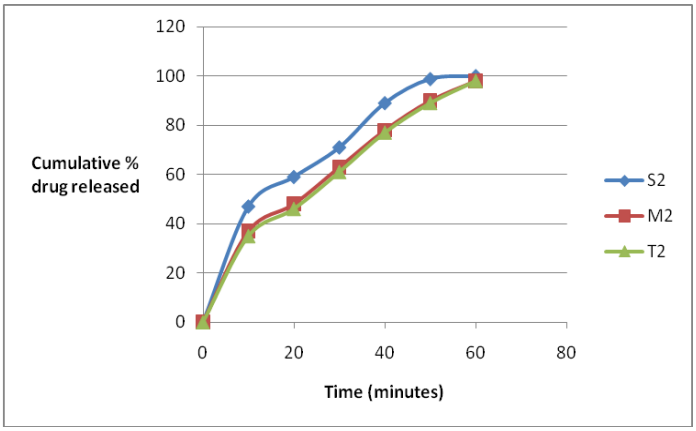
In- vitro dissolution study of the tablets was carried out in USP dissolution apparatus Type-II, using 900ml of phosphate buffer pH 7.2 as a release medium maintained at 37+ 0.5° C with 50 rpm. 5 ml of samples was withdrawn at specified interval and filtered and diluted with phosphate buffer pH 7.2 and assayed spectrophotometrically at 276 nm. The equal volume of fresh medium was immediately replaced to maintain the dissolution volume constant. The amount of drug release at each time interval was calculated from the absorbance of the samples. Three trials were carried out. The percentage drug release was calculated and this was plotted against function of time to find out pattern of drug release.

Figures of Dissolution data:



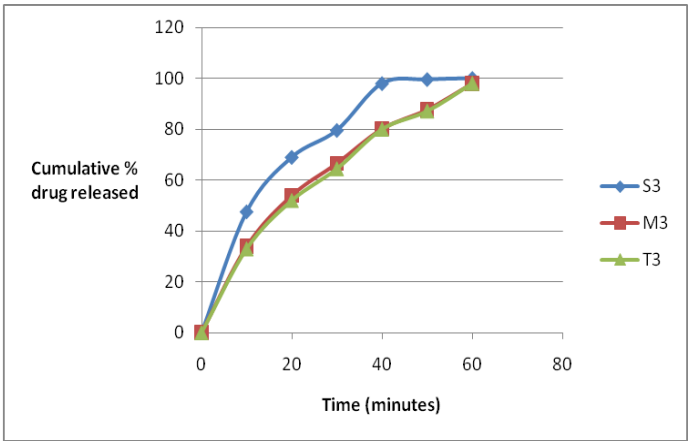
All values are in SD ± n =3

Fig. 1 Comparative dissolution profiles of S1. M1, T1



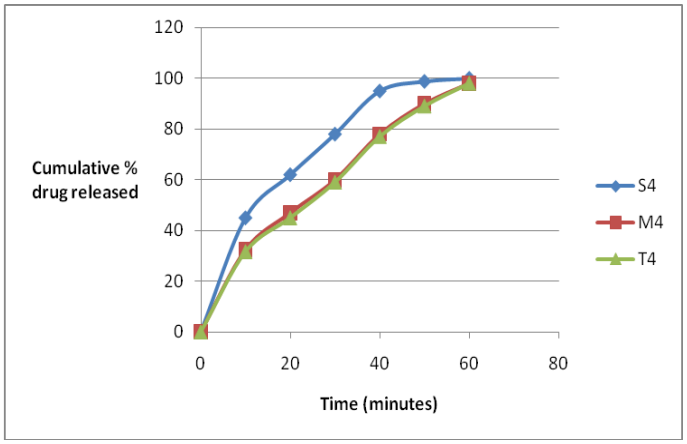
All values are in SD ± n =3

Fig. 2 Comparative dissolution profiles of S2, M2, and T2.



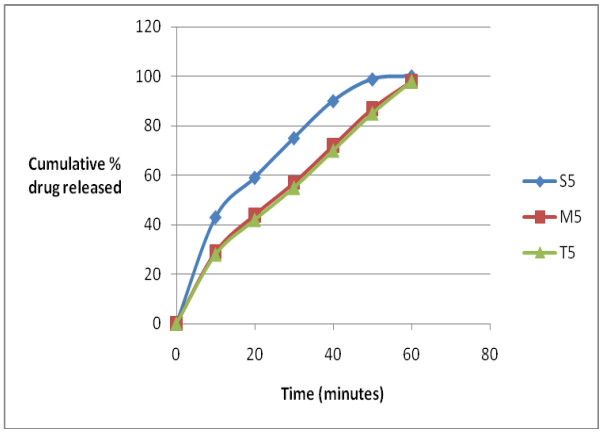
All values are in SD ± n =3

Fig. 3 Comparative dissolution profiles of S3, M3 and T3.



All values are in SD ± n =3

Fig. 4 Comparative dissolution profiles of S4, M4, and T4.



All values are in SD ± n =3

Fig. 5 Comparative dissolution profiles of S5, M5, and T5.

RESULTS AND DISCUSSIONS

Flow properties of powder have inverse relationship with lubricant concentration. The powders with S1, M1 and T1 batch have compressibility index of 9.14, 10.91, and 11.65 respectively. Similarly these batches have angle of repose values of 17, 19 and 18. These results showed that powders had excellent flow property. Whereas, in S2, M2 and T2 batches powders have compressibility index of 11.32, 13.46 and 15.09 and angle of repose of 20, 22 and 21.5. These results showed that powders have good flow property. However, powders having batches of S4 to S5, M4 to M5 and T4 to T5 showed poor flow property. Hence batches of S4 to S5, M4 to M5 and T4 to T5 have resulted in decreased tablets crushing strength.

The increased lubricant level may have been responsible for a reduction in interparticulate friction. This resulted in closer particle packing and densification, thus impeding the flow of powder through the funnel orifice. Excellent flow property for powders with different lubricants had found in the following order: SSF > MS > TALC.

The tablets of S1 to S5 batches have hardness of 6.3, 5.4, 4.8, 4.2 and 3.5. Whereas the tablets of M1 to M5 batches have hardness of 6.5, 5.2, 4.4, 3.6, 2.8 respectively and tablets of T1 to T5 batches have hardness of 6.1, 5, 4.2, 3.4 and 2.6 respectively. These results showed that hardness decreased slightly from batch S1 to S5, whereas hardness values sharply decreased with batches of M1 to M5, and T1 to T5 respectively. The disintegration time for S1 to S5 batches was 3.29, 3.55, 4.33, 5.21 and 6.20 minutes. Whereas for batches of M1 to M5, and T1 to T1 was 3.54, 4.30, 5.17, 6.20 and 7.39 , 3.48, 4.36, 5.26, 6.32, and 7.50 minutes respectively.

The tablets of batches S1 to S5 showed greater amount of drug released than batches of M1 to M5, and T1 to T1. This happened becaused sodium steryl fumarate batch is an inert, hydrophilic lubricant and it does not retard the drug dissolution rate. Because of its greater water penetration capacity than other lubricants, it released drug more effectively. Magnesium stearate and Talc have the tendency to coat the individual particles; hence detrimental effects of these lubricants can be exacerbated.

Sodium stearyl fumarate is a very effective tablet lubricant. The tablets which were prepared with sodium stearyl fumarate had less impact on hardness variation. Similarly tablets of sodium stearyl fumarate had less disintegration time and it released drug more effectively with less time as compared with magnesium stearate and talc.

CONCLUSIONS:

Sodium stearyl fumarate is an effective tablet lubricant. In the concentration of 0.5 to 1.5% concentration sodium stearyl fumarate, magnesium stearate and talc had found to be excellent flow property. Beyond 1.5%

concentration of lubricants, flow property of powders in terms of compressibility index was found to be poor. The tablets containing sodium stearyl fumarate had less impact on hardness variation. Similarly tablets of sodium stearyl fumarate had less disintegration time and it released drug more quickly as compared with magnesium stearate and talc. Future aspects includes, sodium stearyl fumarate is inert, hydrophilic lubricant for all solid oral dosage form and plays a very important role in all types of immediate released preparations, oral disintegrating and mouth dissolving tablets.

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