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EVALUATION OF SOY LECITHIN AS A DIRECT COMPRESSION VEHICLE AND SUBSTITUTE OF LUBRICANT IN DICLOFENAC SODIUM TABLETS

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ABSTRACT

In the current study soy lecithin powder was evaluated as a direct compression vehicle (DCV) and as a substitute of lubricant in the manufacture of directly compressed diclofenac sodium tablets. In the study two formulations, F1 and F2 of diclofenac sodium were prepared by direct compression method. F1 was prepared with the blend of drug, MCC and magnesium stearate where as F2 was prepared with the blend of drug, soy lecithin powder and a small proportion of MCC. The prepared formulation blends were subjected to pre-compression studies such as; angle of repose, bulk density, tapped density, compressibility index and Hausner's ratio. The blends were subjected for direct compression. The prepared tablets of F1 and F2 were subjected to post compression studies like weight variation, hardness, friability, disintegration and dissolution**.** From the data the drug release profile from F1 and F2 were studied. The results of F1 are compared with obtained results F2. On comparison the pre-compression parameters of F2 were nearly same as those of F1 and the post compression parameters were found to be slightly better than those of F1 by resulting in slightly better release of the drug. The study revealed that soy lecithin could function

both as a direct compression vehicle and lubricant in tablets and shown enhanced bioavailability of the drug during *in-vitro* dissolution study.

KEY WORDS: Soy Lecithin, Direct Compression Vehicle, Lubricant, enhanced bioavailability.

INTRODUCTION

Among all the oral dosage forms tablets are most commonly used dosage forms. The ease of manufacturing, convenience in administration, accurate dosing, and stability compared to oral liquids; tamper-proofness compared to capsules; and safety compared to parenteral dosage forms makes tablets a popular and versatile dosage form [1]. In the manufacture of tablets, there are several excipients which are added to aid the manufacturing process and to ensure stability of the formulation. Excipients chosen should suit the patients in terms of acceptance and bioavailability. Various excipients like lubricant, binders and glidants are used duding tablet making to provide their essential manufacturing functions. To aid in product identification and patient acceptance of the manufactured drug, flavours and colourants are added. Disintegrating agents and hydrophilic polymers are be added to optimize or modify the drug release. For enhancing the stability of the product, antioxidants or UV absorbers are used as excipients. There are several ways to compress tablets, either by wet granulation, dry granulation or direct compression. However for the current study, direct compression method of formulating tablets was preferred due to its advantages. One of these advantages is cost effectiveness because it requires less space, time, labor and energy. Apart from that it is also suitable for moisture and heat sensitive active ingredients, due to the fact that it eliminates wetting and drying steps and increases the stability of them. The changes in dissolution profiles are less likely to occur in tablets made by direct compression after storage compared to those made from granulations[2]. Faster dissolution is observed by tablets prepared by direct compression and can be used to prepare tablets with poorly soluble API. This is because the tablets prepared by direct compression disintegrate into API particles instead of granules that directly come into contact with dissolution fluid and therefore exhibits comparatively faster dissolution. Apart from that less wear and tear of punches occur because direct compression can avoid the high compaction pressure involved in the production of tablets by slugging or roller compaction[2]. Further advantages are such as less contamination since the ingredients are processed for a shorter period of time and there is no water present, unlike wet granulation which would increase the chance of

microbial growth, the chance for contamination is low[2]. Lastly, tablets produced by direct compression are easier to validate because validation and documentation requirements are reduced and the process will become easier because of the lesser unit operations[2].

Diclofenac sodium is a widely used non-steroidal anti-inflammatory drug (NSAID). It is a benzeneacetic derivative and its chemical name is 2-[2,6-dichlorophenyl)amino]benzeneactic acid, monosodium salt. Its molecular formula is $C_{14}H_{10}C_{l2}NNaO_2$ [3]. It is slightly hygroscopic in nature and is only sparingly soluble in water but completely soluble in methanol[3].

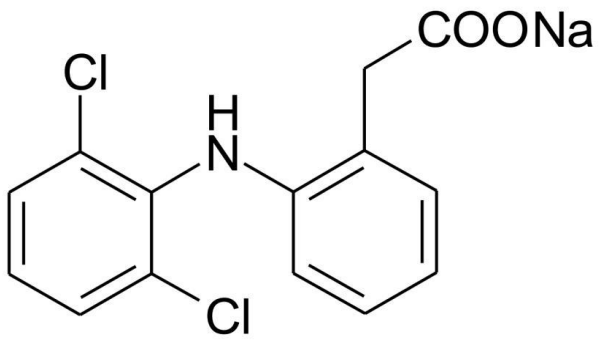

Figure: 1.Chemical Structure of Diclofenac Sodium

Diclofenac sodium is mainly used as an antirheumatic, antipyretic, analgesic and also has effect on osteoarthritis. The primary mechanism responsible for its anti-inflammatory, antipyretic, and analgesic action is inhibition of prostaglandin synthesis by inhibition of cyclooxygenase (COX) which also decreases prostaglandins in the epithelium of the stomach, making it more sensitive to corrosion by gastric acid which is the main side effect of Diclofenac sodium[4].

The major limitation of NSAID use is the risk of serious upper gastrointestinal events, including bleeding, perforation and obstruction, which occur in 1%–2% of users [5]. The fact that NSAID can also cause serious lower gastrointestinal complications, including bleeding, perforation, stricture, anemia and hypoalbuminemia is certainly not appreciated by both prescribers and patients and it also reduces patient compliance. Although the reported incidence of NSAID related to lower gastrointestinal complications varies from 14% to 40%, the true incidence is uncertain because patients and doctors often do not realize that there is a problem[6]. Lecithin is a naturally occurring emulsifier that can be found in soybeans, eggs, sunflower seeds and canola seeds. The chemical nomenclature of lecithin is complex and some literature sources refer to it as 1,2-diacyl-sn-glycero-3-phosphocholine[7]. Lecithin is made by purifying phospholipids of these

naturally occurring products and is used for a variety of purposes such as an emulsifying agent, wetting and instantizing agents, viscosity modifier, extrusion aid, separating agent, and as nutritional supplement. Lecithin has the unique hydrophobic and hydrophilic surface active properties of phospholipids. The phospholipids present in lecithin are phosphatidylcholine, phosphatidylethanolamine, phosphatidyl-inositol and phophatidic acid. In pharmaceuticals, formulations made with phospholipids have several advantages like enhanced bioavailability of drugs with low aqueous solubility or low membrane penetration potential, improvement or alteration of uptake and release of drugs, protection of sensitive active agents from degradation in the gastrointestinal tract, reduction of gastrointestinal side effects of non-steroidal anti-inflammatory drugs and even masking the bitter taste of orally administered drugs[8]. There have been various studies conducted evaluating the benefits of lecithin. Among them, the research by Jiang et al. demonstrated the inhibition of cholesterol absorption in diets which are rich in phosphatidylcholine. This study suggests that the high degree of saturation of acyl groups of the soybean phosphatidylcholine decreases the cholesterol intestinal absorption. Lecithin is one of the natural elements that have dispersing properties and can emulsify fat, avoiding its absorption. Lecithin is capable of reducing LDL-cholesterol. It also promotes the HDL-cholesterol synthesis[9]. Apart from being used to reduce cholesterol and triglycerides and protect the liver in the prevention of kidney stone formation, it is also used as a tonic for the nervous system and brain activities. The Food and Drug Administration (FDA) USA, and the World Federation of Cardiology recommended the use of 25 grams per day of soy protein, which corresponds to approximately 60 g of soybeans for cardiovascular disease prevention[10]. In this study, soy lecithin was evaluated as an excipient, that is as a DCV and substitute of lubricant in the manufacture of Diclofenac sodium tablets by direct compression.

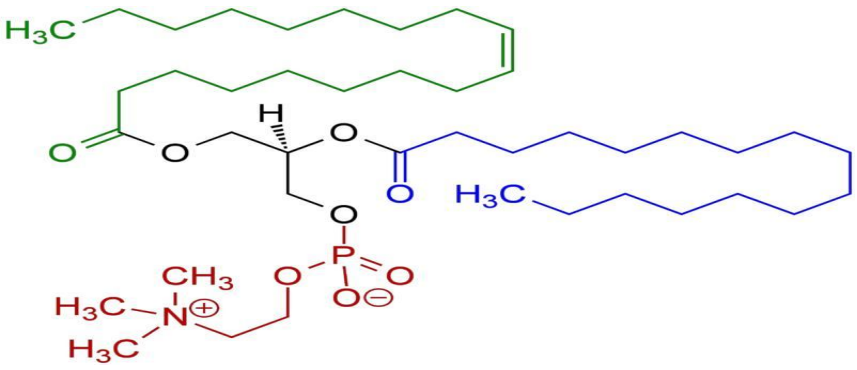

Figure: 2.Structure of Lecithin Phospholipid

MATERIALS AND METHODS

MATERIALS

Soy Lecithin was purchased from Radiant Code Sdn. Bhd., Diclofenac Sodium was obtained as gift sample from Ranbaxy, Microcrystalline Cellulose and Magnesium Stearate and MCC was supplied by AMU.

METHODS

The tablet formulations F1 and F2 were made by direct compression. The drug and excipients were mixed together by geometric dilution and passed through 500 micron sieve. The mixture is compressed by using tablet press. Pre and post formulation studies were conducted. Each parameter was tested and repeated three times. The mean and standard deviation were obtained from the results. The results obtained were tabulated and compared. The formulae of F1 and F2 are represented in Table: 1.

Table: 1.The ingredients used for F1 and F2

Formulation	Diclofenac Sodium (mg)	Microcrystalline Cellulose (mg)	Soy Lecithin (mg)	Magnesium Stearate (mg)
F1	50	247	-	3
F2	50	50	200	-

PRE-COMPRESSION STUDIES

Pre-formulation studies were conducted on mixtures of drug with soy lecithin and drug with microcrystalline cellulose. The flow properties of both the blends were determined and compared.

1. Angle of repose

For angle of repose (θ), the blend was poured through the walls of a funnel, which was fixed at a position, using a retort stand, such that its lower tip was at a height of exactly 2.0 cm above hard surface. The blends were poured till the time when upper tip of the pile surface touched the lower tip off the funnel. The radius was calculated. The $\tan^{-1}$of the (height of the pile/radius of its base) was calculated as the angle of repose.

$\tan \theta = h/r$;Where, h is height of powder cone, r is radius of powder cone.

2. Bulk density and tapped density

The blend was weighed and poured gently through a glass funnel into a graduated cylinder. The volume of the blend was noted and the bulk density was calculated. Using the same blend in the cylinder, it was then tapped using the tapped density apparatus set to 100 taps. The tapped density is obtained and calculated. The bulk density (BD) and tapped density (TD) were calculated using the formula below.

Bulk density= weight of the blend/ untapped volume

Tapped density= weight of the blend/tapped volume

3. Hausner's ratio and compressibility index

Hausner's ratio (HR) and Carr's compressibility index (IC) were calculated according to the two standard equations given below:

HR = TD/BD

IC = (TD- BD)/TD × 100

CALIBRATION CURVE

100 mg of diclofenac sodium was taken in a conical flask & dissolved in 100ml of pH 6.8 phosphate buffer.10 ml of this solution was taken and diluted up to 100 ml with pH 6.8 phosphate buffer. The aliquots of 1, 2, 3, 4, & 5ml solution were prepared in 10 ml of pH 6.8 phosphate buffer. The absorbance was measured at 283nm by using UV visible spectrophotometer & the graph of concentration (µg/ml) versus absorbance was plotted as standard calibration curve.

Table: 2.Observations of calibration curve

Concentration(µg/ml)	Absorbance
10	0.280200 ± 0.0002646
20	0.520133 ± 0.0001528
30	0.710467 ± .0005686
40	0.891100 ± 0.0011533
50	1.051933 ± 0.0035233

***Mean ± standard deviation *n=3**

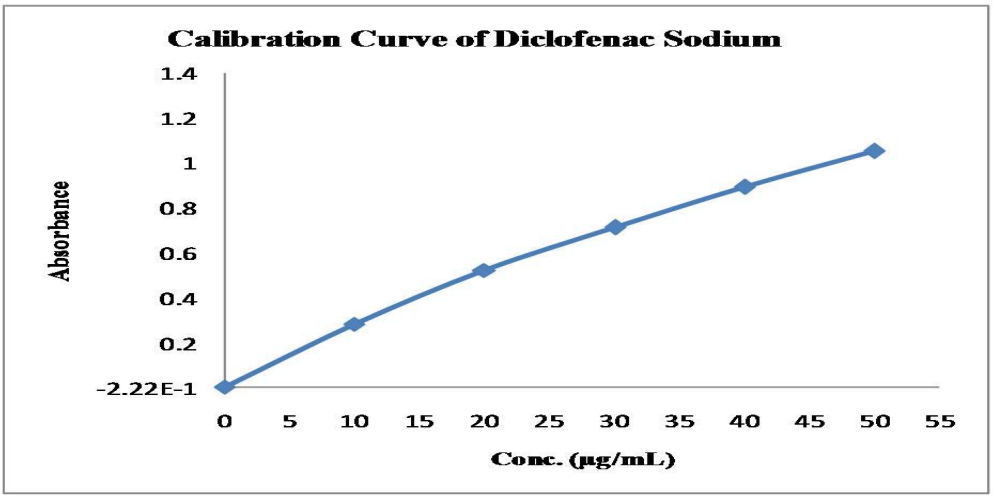

Figure: 3.Calibration Curve of Diclofenac Sodium

POST COMPRESSION PARAMETERS

1. Uniformity of weight

Twenty tablets were taken randomly and their individual weights were determined on a digital weighing balance. The average weight of the tablet was calculated from the collective weight. The weights were compared for uniformity.

2. Friability

The friability of randomly picked six tablets was measured using a Roche Friabilator. Six pre-weighed tablets were rotated at 25 r.p.m. for 4 minutes. The tablets were then reweighed after removal of fines and the percentage of weight loss and the friability were calculated. Friability = [(Initial weight-Final weight) / Initial weight)] ×100 [%]

3. Hardness

Hardness of the prepared tablets of F1 and F2 were determined by using a Pfizer hardness tester and the values were compared.

4. Disintegration time

Disintegration time was measured according to the USP 701. One tablet was placed in each of the 6 tubes of the basket in 900mL of water and the temperature was maintained at 37 ± 2°C. The disintegration time of 6 individual tablets were observed and recorded.

5. Dissolution

Dissolution rate was studied by using USP type II apparatus rotated at 75 rpm in 900mL of phosphate medium. Temperature of the dissolution medium was maintained at 37±0.05°C. Aliquot of the dissolution medium was withdrawn at specific time interval. The absorption of the solution was checked out by UV spectroscopy at 283nm and drug content was determined from the standard curve. The dissolution rate was studied for both formulations and the results were compared.

RESULTS

Table: 3.Pre-compression Parameters

Parameters	F1	F2
Bulk Density (g/mL)	0.004583	0.4346
Tapped Density (g/mL)	0.35700	0.5020
Compressibility Index (%)	13.1666	13.4066
Hausner's Ratio	1.1510	1.1543
Angle of Repose (°)	28.5900	28.2263
*n=3		

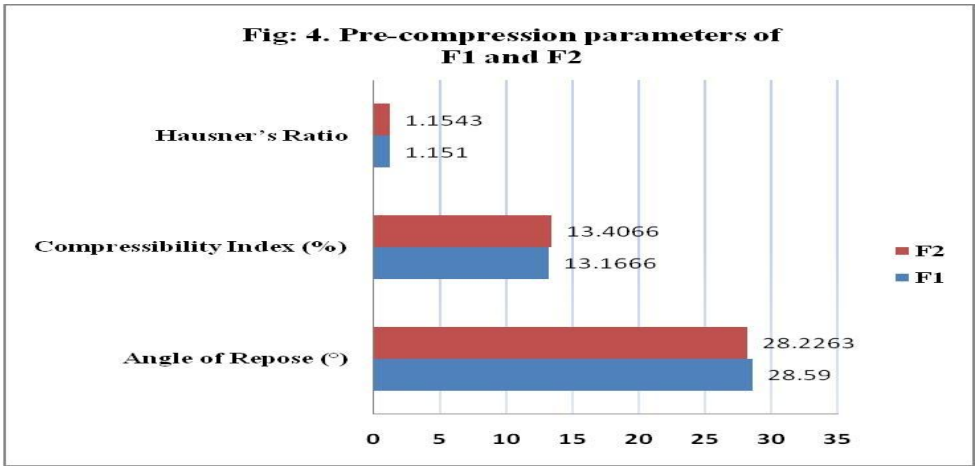

Figure: 4.Pre-compression Parameters

Table: 4.Post-Compression Parameters

Parameters	F1	F2
Weight variation (%)	3.64	3.44
Friability (%)	0.2733	0.2233
Hardness (Kg)	6.2	5.8
Disintegration Time (s)	43.3	39.0
*n=3		

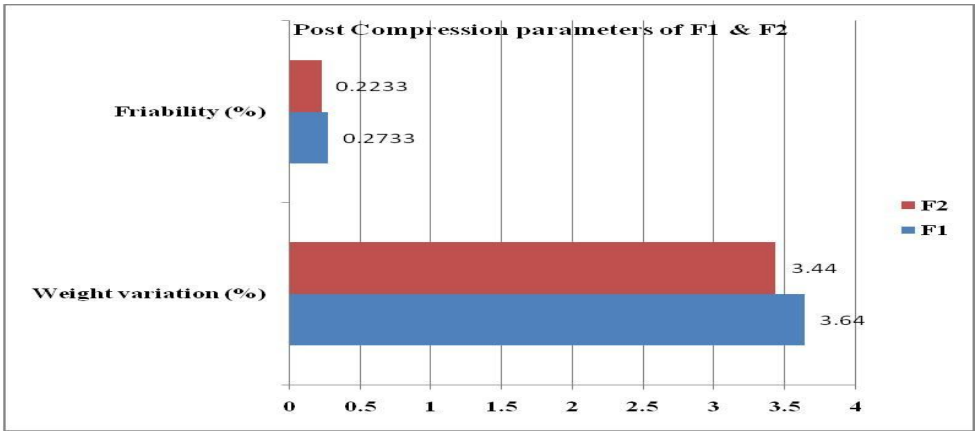

Figure: 5.Post Compression parameters (Friability & Weight variation) of F1 & F2

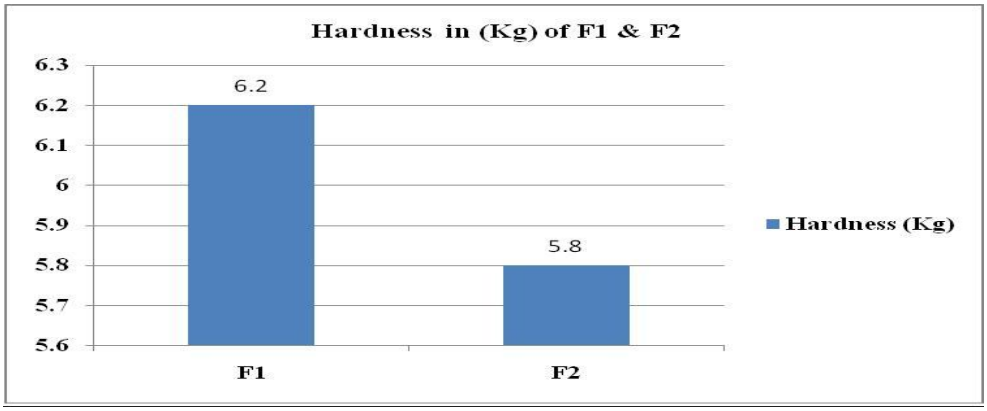

Figure: 6. Post Compression parameters (Hardness) of F1 & F2

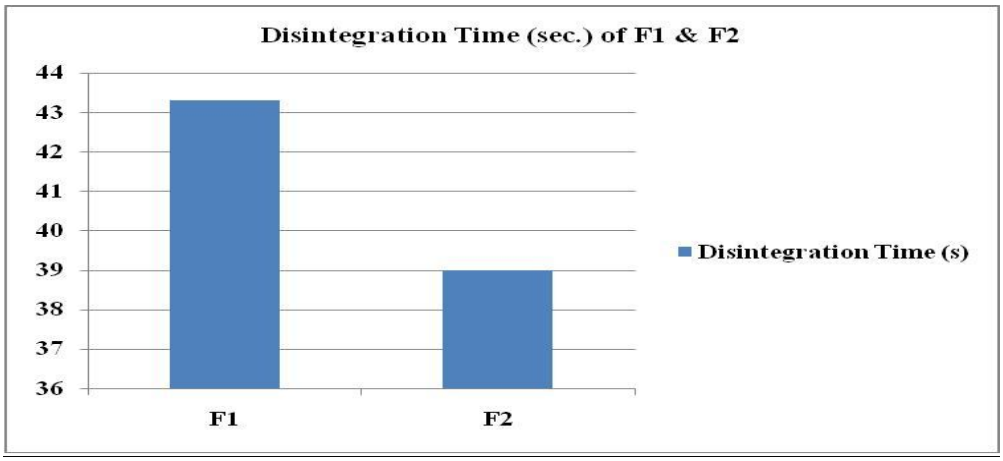

Figure: 7. Post Compression parameters (Disintegration Time) of F1 & F2

Table: 5.Dissolution profile of F1

Time (mins)	Absorbance	Conc. (µg/mL)	Conc. in 900mL (mg/mL)	% Concentration release
5	0.051100±0.0003606	0	0	0
10	0.269100±0.0002000	17	15.3	30.6
15	0.442467±0.0001528	25	22.5	45.0
20	0.623100±0.0002000	29	26.1	52.2
25	0.801100±0.0002000	38	34.2	68.4
30	1.018033±0.0053126	50	50	100

***Mean ± standard deviation *n=3**

Table: 6.Dissolution profile of F2

Time (mins)	Absorbance	Conc. (µg/mL)	Conc. In 900mL (mg/mL)	% Drug release
5	0.030000±0.0011000	0	0	0
10	0.389000±0.0010000	20	18.0	36.0
15	0.581033±0.0015280	27	24.3	48.6
20	0.781133±0.0002517	36	32.4	64.8
25	0.984033±0.0001528	48	43.2	86.4
30	1.156133±0.0002517	40	50.0	100

***Mean ± standard deviation *n=3**

Table: 7.Percentage Drug Release from F1 and F2

Time (Min)	% Drug release from F1	% Drug release from F2
5	0	0
10	30.6	36.0
15	45.0	48.6
20	52.2	64.8
25	68.4	86.4
30	100	100

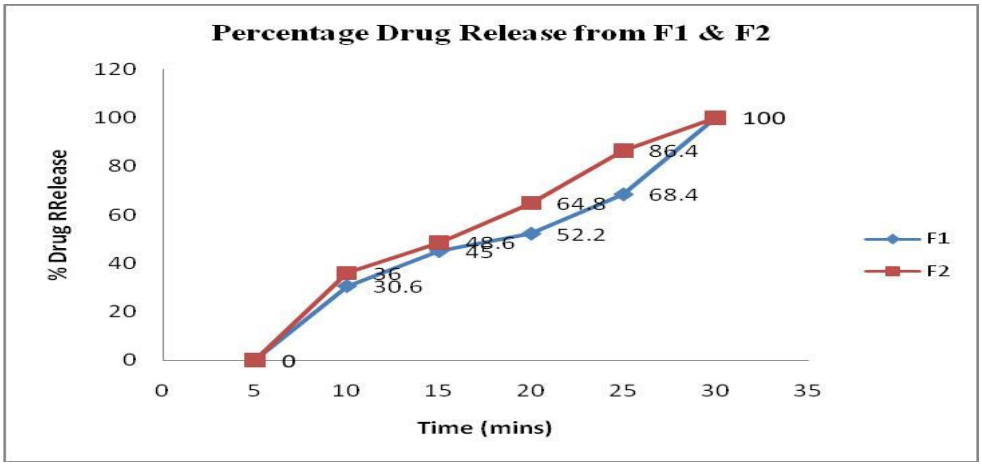

Figure: 8.Percentage Drug Release Profiles of F1 and F2

DISCUSSION

The present study was undertaken to evaluate soy lecithin as a direct compression vehicle and as a substitute of lubricant in directly compressed Diclofenac sodium tablets. Two formulations were made F1 and F2. The formulation F1 was prepared with MCC as direct compressive vehicle (DCV) and magnesium stearate as a lubricant and the formulation F2 was prepared with Soy lecithin powder as DCV as well as the same as a lubricant and a small proportion of MCC as glidant. Pre-compression parameters of F1 and F2 blends were determined and compared. The angle of repose of F2 blend was found to be 28.2263 and that of F1blend was found to be 28.59 and both blends exhibited good flow property[11]. The bulk density of F2 blend was found to be 0.43467 g/mL and that of F1 blend was 0.004583 g/mL, tapped density of F2 was 0.5020 g/mL and for F1 it was 0.3570 g/mL, with these values the compressibility index (CI) of both blends were calculated. CI for F2 was 13.4066 and for F1 it was found to be 13.1666. The CI of both F2 and F1 were within the range of 12-16% which exhibit good flow [11]. The Hausner's ratio for F2 was found to be 1.1543 and F1 was 1.1510 and a value less than 1.25 exhibit good flow[11] . All these values were represented in Table: 3 and are plotted in the graph which is shown in Figure:4. The pre-compression studies revealed that both F2 and F1 are having good flow properties. Post-compression parameters of both formulations F1 and F2 were determined. The weight variation was found to be 3.64% and 3.44% in batches of F1 and F2. The weight variation in the batch F2 was slightly lower than that in F1 batch. The friability F values were determined as 0.2733% and 0.2233% in F1 and F2 respectively and both were found to be under standard range. All the results of post-compression parameters were shown in Table:4. The parameters of

weight variation and friability of F1 and F2 were compared in the graph and shown in Figure:5.

The hardness of F1 and F2 were found to be 6.2 and 5.8 kg respectively, both the values were observed to be in the standard range. The hardness value of F2 was observed to be slightly lower than the value of F1 and the values of hardness were compared in the graph and shown in Figure:6. Disintegration test was carried out and the average disintegration for F1 was 43 sec and F2 was found to be 39 sec. This shows that tablets of both F1 and F2 batches under go fast disintegration. However the F2 batch has a slightly faster disintegrating time as compared to F1, both were considered under standard limit of disintegration time. The values of DT were shown in Table:4 and they are compared in the graph which was represented in Figure:7. Dissolution studies were carried out and it was noted that complete dissolution of tablets from both the batches occurred within 30 minutes to release 100% of drug and the tablets of F2 batch exhibited faster and higher rate of dissolution during the release rate study on comparison with the tablets of F1 batch. The results of dissolution study of tablets from F1 and F2 were shown in Table:5 & 6 respectively, the same were compared in Table:7 and the comparative release rate of drug from the tablets of F1 and F2 were shown in the graph which was represented in Figure:8.

CONCLUSION

This study revealed that soy lecithin passed all the pre and post compression evaluation tests and it can be a choice of a direct compression vehicle and substitute of lubricant. The flow property of the prepared blend with soy lecithin was as good as the blend with MCC but it has the upper advantage in terms of the dissolution profile. The batch containing soy lecithin (F2) shown a faster dissolution profile of releasing the drug than the tablets of batch with MCC (F1). Since soy lecithin has been shown to reduce gastrointestinal (GI) side-effects, this could prevent gastric irritation caused by diclofenac sodium. There has been a study that showed GI protective effect of soybean phospholipid which reduced gastric mucosal lesions in rats after the treatment with NSAID. Apart from that, soy lecithin will be able to take on two roles, that is as a direct compression vehicle (DCV) and also as a lubricant. The observed benefits of using soy lecithin as a direct compression vehicle resulted in faster and greater release of drug, reduced excipient use, reduced cost and time of manufacture and revealed the potential use of soy lecithin as a direct compression vehicle and a substitute of lubricant in directly compressed tablets of Diclofenac sodium.

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