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Effect of natural polymer on conventional and sustained release properties of indomethacin tablets

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Abstract

The aim of the present study was to evaluate seed flour of *Vigna mungo* (L.) Hepper or Black gram as binding, disintegration nature and sustained release matrix forming material in tablet formulation. The seeds of *Vigna mungo* swell and form gelatinous mass when it comes in contact with water due to its hydrophilic nature. Indomethacin (NSAIDS) was selected as a model drug because of its poor water solubility and short half life. FT -IR studies showed no evidence on interaction between indomethacin and *Vigna mungo*. Conventional /sustained release matrix tablets of indomethacin, was developed by using wet granulation technique. Compressed tablets were evaluated for pharmacopoeias tests and compared with marketed product. The kinetic studies showed that the release of drug from formulation CVF2 follows first order model and formulation SVF1 follows zero order model and anomalous diffusion and explained by Higuchi's model. Selected conventional formulation CVF2 was carried out by anti-inflammatory activity by using plethysmometer. The selected formulations CVF2 and SVF1 was subjected to stability studies for three months at 45ºC temperature with RH 75±5%, and showed stability with respect to release pattern.

Key words: *Vigna mungo*, phyto-physicochemical, indomethacin, conventional /sustained release matrix tablets, evaluation, anti-inflammatory activity and stability

Introduction

Non steroidal anti-inflammatory drugs (NSAIDs) are highly effective in the treatment of rheumatoid and osteoarthritis but their long term use results in gastrointestinal (GI) toxicity in a large number of cases like ulceration and stricture formation in esophagus, stomach and duodenum leading to severe bleeding, perforation and obstruction (Rang *et al*., 2003). Indomethacin, having gastrointestinal side effects ranging from mild dyspepsia to gastric bleeding and its short plasma half-life (1-3 h). Indomethacin is an ideal candidate for preparing extended or controlled release drug products that can potentially avoid drug release in upper position of the GI tract (Kathiresan *et al*., 2010).

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The seed mucilage are pharmaceutically important polysaccharides with wide range of applications such as thickening, binding, disintegrating, suspending, gelling, emulsifying, stabilizing agents and also as release retardants. They are normal products of metabolism formed within the cell and they represent storage material that consists of sugar and uronic acid units. Because of its colloidal nature and viscosity, they can be used to suspend insoluble substances in liquids and help in preventing sedimentations in suspensions. The *Vigna mungo* seed mucilage used to impart cohesive qualities to the powdered material during the production of tablets. The seeds of *Vigna mungo* swell and form gelatinous mass when it comes in contact with water due to its hydrophilic nature (Onyilagh *et al*., 1982). Several matrixes based controlled release products of indomethacin have been reported based on the use of either hydrophilic (HPMC or Carbopol) and/or hydrophobic polymers (EC). HPMC has been employed for preparing sustained release matrix tablets by wet granulation process. In the present study, it was envisaged to design sustained release formulation of

indomethacin with *Vigna mungo* so as to minimize initial drug release in stomach that will reduce the possible gastro irritant and ulcerogenic effects of the drug. At the same time, there would be no effects of the drug. At the same time, there would be no compromise on the biopharmaceutical profile of the drug as indomethacin is reported to be well absorbed throughout the GI tract.

The *Vigna mungo* seed powder pharmaceutically important polysaccharides with wide range of applications such as thickening, binding (Bodempudi Sravani *et al.*, 2011), disintegrating, suspending, gelling, emulsifying, stabilizing agents and as release retardants (Indranil Kumar Yadav *et al.*, 2009). Hence, in the present study was to evaluated phytochemical properties of *Vigna mungo* seed powder and has been evaluated for its binding, disintegration nature and swelling properties in tablets, using indomethacin as a model drug. The conventional form of indomethacin was developed to immediate drug release to reduce the inflammation. The sustained release formulation of indomethacin was developed to reduce gastric mucosal damage and other toxicities of the drug.

Preparation of Vigna mungo seed powder

The dehusked seeds of black gram were properly washed with distilled water and dried in a oven at temperature less than 50^0C. The dried seeds were powdered in a ball mill and passed through # 120 sieve, using sieve shaker and stored in desiccator until further use.

Phyto-physicochemical properties and characterization of Vigna mungo seed powder

The phyto-chemical examinations such as ruthenium red test, molisch test, and iodine test confirm the presence of mucilage. The physicochemical properties such as loss on drying and viscosity was determined according to Indian pharmacopoeial procedure**.** The pH of 1% solution was measured using a digital pH meter by dispersing the black gram mucilage in 25ml of distilled water.

Micromeritic properties of Vigna mungo seed powder

The seed powder was studied for various micromeritic properties such as bulk density, tap density, angle of repose, carr's index and hausner's ratio.

Drug-excipient compatibility studies

Compatibility studies were carried out to know the possible interactions between indomethacin and *Vigna mungo* used in the formulation. Physical mixtures of drug and excipient were prepared to study the compatibility. Drug polymer compatibility studies were carried out using FT-IR (Shimadzu 160a, Kyoto, Japan) spectroscopy. IR spectrum of pure drug and polymers was seen in between 500- 4000 cm-1.

Formulation of indomethacin conventional tablets and sustained release matrix tablets

The conventional tablets were prepared by wet granulation technique using varying concentrations of *Vigna mungo* seed powder, used as a binder and disintegrant agent as mentioned in Table 1**.** To the indomethacin, mucilage powder, dicalcium phosphate, and starch added and granulated using isopropyl alcohol as granulating agent. The wet mass was passed through sieve no 12 and the granules obtained were dried at 45^0C for 30 minutes. The dried granules were subjected to dry screening by passing through sieve no 24 and then granules were lubricated with mixture of talc and magnesium stearate. The granules were compressed into tablets using 6mm concave punch in rotary tablet machine Minipress-22 (REMIK Ltd). The batch size of 40 tablets was prepared.

Sustained released matrix tablets of indomethacin were prepared by using different drug : polymer ratios *viz*., 1:1, 1:2, 1:3 and 1:4, mentioned in Table 2. *Vigna mungo* seed powder was used as matrix-forming material, while poly-vinyl pyrrolidone was used as a binder. Tablets prepared with HPMC 50Cps as matrix forming material for the comparative study. Magnesium stearate and talc were incorporated as lubricant. All ingredients were passed through a #100 sieve, weighed and blended. The tablets were prepared by wet granulation technique. Isopropyl alcohol was used as granulating agent and it was added slowly to the powder blend, and kneading was performed for few minutes until formation of wet mass. The wet mass passed through a #16 sieve and dried at 50^0C in a hot air oven for 3-5 h. The dried granules were re-sieved through a #20 sieve and thoroughly mixed with the lubricants. The lubricated granules were compressed by using a 6mm single station tablet punching machine, using flat faced punches. The batch size of 40 tablets was prepared.

Drug content of indomethacin conventional tablets and sustained release matrix tablets

Twenty tablets were weighed and powdered. Weighed accurately a quantity of the powder containing 25 mg of indomethacin was shake with 10 mL of water for 10 minutes diluted to 100 mL with methanol and filtered. To 5.0 ml of the filtrate add sufficient of a mixture of equal volumes of methanol and phosphate buffer pH 7.4 to produce 100 ml. Measure the absorbance of the resulting solution at the maximum at about 320 nm.

Swelling behavior of indomethacin sustained release matrix tablets

The extent of swelling was measured in terms of % weight gain by the tablet. The swelling behavior of indomethacin sustained release tablets based on different matrices were studied. The swelling of matrices was monitored by immersing the tablet into a basket of USP2 dissolution rate test apparatus

containing 900 ml of dissolution medium (pH 7.4 phosphate buffer) maintained at 37±0.5°C for 12 h. at 50 rpm. At the end of 2 h, the tablet was withdrawn, kept on tissue paper and weighed then for every 2 h, till the end of 12 h, % weight gain by the tablet was calculated by formula.

$$S.I = \{(Mt-Mo) / Mo\}x100.$$

where, S.I = swelling index, Mt = weight of tablet at time 't' and Mo = weight of tablet at time t = 0. Swelling behavior of sustained release matrix tablets were represented in Figure 5.

In vitro drug release studies of indomethacin conventional tablets

The dissolution rate of indomethacin from the tablets was studied in 900 ml of 7.4 pH phosphate buffer , using Electrolab-TDT-08L USP2 dissolution test apparatus with paddle stirrer at 75 rpm. A temperature of 37°C + 1°C was maintained throughout the study. One tablet containing 25 mg of indomethacin was used in each test. At a predetermined time interval (5, 10, 15, 30, 45, 60, 75, 90,105 and 120 minutes), samples were withdrawn and filtered through a filter (0.45 µm). Dissolution sample withdrawn (5ml) at each time was replaced with fresh dissolution sample. Suitably diluted and assayed for indomethacin at 320 nm, respectively. The dissolution experiments were conducted in triplicate.

In vitro drug release studies of indomethacin sustained release matrix tablets

The dissolution rate of indomethacin from the tablets was studied in 900 ml of acidic buffer 1.2 pH for first two hours and remaining studied (up to 24 h) in 7.4 pH phosphate buffer using Electrolab-TDT-08L USP2 dissolution test apparatus with paddle stirrer at 75 rpm. A temperature of 37°C + 1°C was maintained throughout the study. One tablet containing 75 mg of indomethacin was used in each test. At a predetermined time interval, samples were withdrawn and filtered through a filter (0.45 µm). Dissolution sample withdrawn (5ml) at each time was replaced with fresh dissolution sample. Suitably diluted and assayed for indomethacin at 320 nm, respectively. The dissolution experiments were conducted in triplicate.

Kinetic release studies of indomethacin conventional and sustained release matrix tablets

The Korsmeyer and Peppas equation was used to analyze the data obtained from the *in vitro* release studies to evaluate the kinetic models and release mechanism of indoethacin from the matrices (Peppas and Sahlin, 1989).

$$Mt/M" = ktn$$

where *Mt*/*M*" is the fraction of drug release at time *t*, *k* is constant incorporating the properties of the macromolecular polymeric system and the drug. The *n* is an exponent used to characterize the transport mechanism. For example, $n = 0.45$ for Case I or Fickian diffusion, $0.45 < n < 0.89$ for anomalous behavior or non-Fickian transport, $n = 0.89$ for Case II transport, and $n > 0.89$ for Super Case II transport. Fickian diffusional release occurs by the usual molecular diffusion of the drug due to a chemical potential gradient (Higuchi *et al*., 1969). Case II relaxational release is the drug transport mechanism associated with stresses and state-transition in hydrophilic glassy polymers, which swell in water or biological fluids. This term also includes polymer disentanglement and erosion.

Anti-inflammatory activity

Anti-inflammatory activity was measured by carrageenan induced rat paw edema model employing plethysmometer apparatus to measure the paw thickness (Sharma *et al*., 2004). Albino rats (supplied by M/S Mahaveer enterprise, Hyderabad, Andhra Pradesh) of either sex, weighing between 150 - 200 gm were used for the experiment. Animal housing and handling were in accordance with the guidelines of the Committee for the Purpose of Control and Supervision on Experiments on Animals. These pharmacodynamic studies were carried out in the Pharmacology laboratories of the Malla Reddy College of pharmacy, which is approved by the institutional animal ethics committee and CPCSEA (Regd.No.CPCSEA/1217/MRCP/2004) for experimentation on animals. The animals were divided into three groups of six animals each (n = 6). Each group of animals was given the following treatments (control, pure indomethacin, formulation CVF2). One hour after treatment, 0.1 ml of 1 % carrageenan suspension was injected subcutaneously into the subplantar tissue of the left hind foot and 0.1 ml of normal saline was injected into the subplantar tissue of the left hind foot. The first group is control group. The second group will be treated with indomethacin 25 mg/kg of body weight (p.o). The 3rd group will be treated with conventional formulation of indomethacin (CVF2). The thickness of both the paws of each rat, lower and upper surface was measured using Plethysmometer apparatus during the course of the experiment. The paw thickness was determined at 0, 0.5, 1, 2, 3, 4, 5 and 6 h after induction of inflammation. The % paw edema was calculated by following equation:

$$\% \text{ Paw edema} = \mathbf{[Y_t - Y_0 / Y_t] \times 100}$$

Where, Y_t = paw thickness at time't' in hours (after injection) and Y_0 = paw thickness at time '0' (before injection) The percent increase in paw thickness was determined for a period of 6 h. The percent inhibition of paw edema thickness is calculated by using following equation.

$$\% \text{ Paw edema inhibition} = \mathbf{[Y_t - Y_c / Y_t] \times 100}$$

Where, Yt = Mean increase in paw thickness in groups tested with test compounds, and Yc = Mean increase in paw thickness in control.

Accelerated stability studies of conventional and sustained release tablets of indomethacin

Accelerated stability study was carried out to observe the effect of temperature and relative humidity on optimized formulations (CVF2/SVF1) by keeping at 40°C, in airtight high density polyethylene bottles for three months, at RH 75±5%. Physical evaluation and *in vitro* drug release was carried out each month for three months.

Results and Discussion

Phyto and physicochemical tests of Vigna mungo seed powder

The *Vigna mungo* seed powder was employed to rhuthenium red test obtained pinkishred colour indicates the presence of mucilage. In molisch test pinkish red ring formed it indicates the presence of carbohydrates, in iodine test observed blue spots under microscopic study indicates the presence of polysaccharides and in mayer's test no colour change its indicates the absence of alkaloids. Loss on drying of *Vigna mungo* seed powder was found to be 1.8% and pH of 1% solution was found to be 7.

Micromeritic properties of Vigna mungo powder

Bulk density of *Vigna mungo* seed powder was found to be 0.62 gm/ml, Tapped density of *Vigna mungo* seed powder was found to be 0.96 gm/ml, Angle of repose of *Vigna mungo* powder was found to be 30.3^0 it indicates good flow. Carr's index was found to be 23.5 and Haussner's ratio was found to be 1.2. It indicates the free flowing.

FT-IR *Spectroscopy*

The IR spectral analysis of indomethacin, *Vigna mungo* and the physical mixture of Indomethacin :*Vigna mungo* were performed, indomethacin spectra showed absorption bonds at 3447 cm^{-1} due to N=H, 3500 - 3300 (m)1717.14 due to C=O (1750-1700), 1479 due to C=C stretching (1450-1600) 751 due to C-Cl stretching (540-760), 1183 due to C-N stretching (1180-1360), 1299 due to C-COOH (1250-1300), and, physical mixture of indomethacin and *Vigna mungo* spectra showed characteristic absorption bonds at 3400 $cm^{"1}$ was partially reduced; as was expected, but the main indomethacin characteristic absorption bands were not affected and shown in Figure 2. The FT-IR spectra of indomethacin and physical mixtures of drug and polymers reveal no physical and chemical interaction between drug and polymers.

Micromeritic properties of indomethacin conventional tablets and sustained release tablets

Flow ability of the granules was evaluated by determining the angle of repose and Carr's Index(CI), was found to be 28.6^0 to 32.8^0 CI was found to be 10.7 to 15.7 because it is a prerequisite to obtain solid dosage form with an acceptable weight variation. According to the literature data excellent flow properties are seen for granules with a compressibility index CI, between 15–25.The compressibility index of the different granulations ranged between 14.3 and 26.1 and therefore indicate their suitability for tabletting. Also the granulations showed acceptable angle of repose ranged between 28° and 35.5°.

Bulk density was found to be 0.46 to 0.55 gm/ml, and 0.35 to 0.50 gm/ml tapped density 0.554 to 0.622 gm/ml. is a prerequisite to obtain solid dosage form with an acceptable weight variation. According to the literature it indicates indomethacin conventional granules has excellent flow property, and Haussner's ratio was found to be 1.11 to 1.18 and 1.1 to 1.2 it indicates free flowing of indomethacin conventional granules and sustained release granules therefore indicate their suitability for conventional and sustained tabletting. The bulk density was found to be 0.35 to 0.50 gm/ml, tapped density 0.40 to 0.65 gm/ml, angle of repose was found to be 28.4^0 to 40.1^0 it indicates indomethacin sustained release granules has good flow properties, Carr's index was found to be 12.5 to 25.0 it indicates indomethacin sustained release granules has excellent flow properties, Hausner' ratio was found to be it indicates indomethacin has free flowing.

Evaluation of the conventional and sustained release tablet properties

The tablet thickness was found to be 2.1 to 2.6 mm, hardness of the tablets was found to be 3.4 to 4.3 kg/cm^2. It indicates less disintegration time of indomethacin conventional tablets. Friability was found to be 0.10 to 0.13%, disintegration time was found to be 3.2 to 4.5 minutes. It indicates faster dissolution rate of indomethacin conventional tablets and drug content was found to be 93.5 to 99.2% were given in Table 3. The prepared tablets showed good hardness and friability as compared with the tablets prepared using starch binder which confirmed the mechanical resistance of the prepared tablets.

The results of sustained release tablet properties were given in Table 4. The thickness of the tablets was found to be 4.0 to 5.5 mm, hardness was found to be 5.6 to 6.8 kg/cm^2, friability was found to be 0.15 to 0.42% and drug content was found to be 90.9 to 101.2%.

Dissolution profile of indomethacin conventional tablets

Indomethacin conventional tablets release profile is shown in Figure 3. The rate of drug release was found to be minimum in formulation (CVF4) 61.0%. And maximum drug release was found to be 93.4% in formulation (CVF2). It was observed that rate of drug release from all tablet formulations containing *Vigna mungo* seed mucilage (CVF2) was fast when compared to formulations containing starch binder (Figure 3).

Dissolution profile of indomethacin* SR *tablets

Indomethacin release profile of seed flour of black gram based matrix tablets is shown in Figure 4. As regards the effect of

polymer concentration, decrease in drug release rate was observed when seed flour of black gram content in the matrix was increased. This may be due to the reason that the polymer in higher concentrations in the tablets might have produced dense matrix around the drug particles, providing more barriers for them to escape and dissolve. Tablets with Drug–Polymer ratio 1:1 (SVF1) showed 89.9% total drug release at the end of 24 h. However, tablets with greater Drug–Polymer ratio-*viz*., SVF2, SVF3 and SVF4 were found effective in sustaining the drug release beyond 24h. Hence, formulation SVF1 is optimized formulation among seed flour of black gram based matrix tablets. HPMC 50 Cps based matrix tablets of indomethacin were used for comparative study.

The effect of the amount of HPMC 50Cps, *i.e*., Drug–Polymer ratio (1:1, 1:2) on the indomethacin release is shown in Figure 1**.** Indomethacin release decreased as the percent amount of HPMC 50Cps level in the tablet increased. Drug release is controlled by the hydration of HPMC 50Cps, which forms a gelatinous barrier layer at the surface of the matrix. In addition, the resistance of such a gel layer to erosion is controlled by the viscosity grade of the HPMC 50Cps. Dissolution profile of the HPMC 50Cps based matrix tablets showed that at levels of Drug-Polymer ratio (1:2), the profile was close to the profile obtained by seed flour of black gram based matrix tablets SVF1.

Drug release mechanism of indomethacin conventional tablets

The optimized formulation of CVF2 follows first order kinetics, the R^2 was found to be 0.923 and marketed product follows first order release studies, R^2 was found to be 0.986. These values are mentioned in Table 5. The optimized formulation of SVF1 follows zero order kinetics, the R^2 was found to be 0.955 and anomalous diffusion mechanism explained by Higuchi model and drug release close to the marketed product. These values are mentioned in Table 6.

In vivo anti-inflammatory activity of indomethacin in rats

Percentage increase in paw thickness (inflammation) and percentage inhibition of inflammation in control and in rats treated with pure indomethacin and selected formulation CVF2 were calculated. In the control group which received carrageenan, rapid increase in paw thickness (*i.e.*, inflammation) was observed and a maximum increase of 63.5 % at 6h after administration was seen in Figure 6. The % paw edema inhibition was found to be 89.2% with selected formulation CVF2. Indomethacin with *Vigna mungo* polymer exhibited better and faster anti-inflammatory activity than pure indomethacin drug

Accelerated stability studies of conventional tablets and sustained release tablets

To assess the stability of indomethacin conventional and sustain release matrix tablets, tablets of CVF2/SVF1 were stored at 45°/75% RH for 3 months. At the end of the study period, the formulation was observed for no changes in physical appearance, color, drug content and drug release characteristics.

Conclusion

The results of the present study show that formulations containing the minimum concentration of 2.0% *Vigna mungo* powder as binding agent show short disintegration and fast dissolution including good physico-mechanical properties. These suggest that black gram powder could be useful as an alternative binding and disintegrating agent for indomethacin tablet production.

The present study revealed that *Vigna mungo* powder appears to be suitable for use as a release retardant in the manufacture of once daily sustained release matrix tablets because of its good swelling, good flow and suitability for matrix formulations. From the dissolution study, it was concluded that *Vigna mungo* powder can be used as an excipient for making once daily sustained release.

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Table 1. Formulation of indomethacin conventional tablets

Ingredients(mg)	CVF1	CVF2	CVF3	CVF4	CSF1	CSF2
Indomethacin	25	25	25	25	25	25
Vigna mungo	5	10	20	30	-	-
Starch	-	-	-	-	10	20
Dibasic calcium phosphate anhydrous	65	60	50	40	60	50
Talc	3	3	3	3	3	3
Magnesium stearate	2	2	2	2	2	2
Total tablet weight (mg)	100	100	100	100	100	100

Table 2. Formulation of indomethacin sustained release tablets

Ingredients (mg)	SVF1	SVF2	SVF3	SVF4	SHF1	SHF2
Indomethacin	75	75	75	75	75	75
Vigna mungo	75	150	225	300	-	-
HPMC 50Cps	-	-	-	-	75	150
PVP K30	2% w/w	2%	2%	2%	2%	2%
Talc	1%w/w	1%	1%	1%	1%	1%
Magnesium Stearate	1%w/w	1%	1%	1%	1%	1%

Table 3. Evaluation of the indomethacin conventional tablets properties

Formulations	Avg. Wt. of Tablet (mg)	Thickness (mm)	Diameter (mm)	Hardness (kg/cm^2)	Friability (%)	Disintegration (min.)	Drug content %
CVF1	100.5 ± 0.25	2.1 ± 0.2	6.2± 0.12	3.8 ± 0.5	0.101 ± 0.01	3.5 ±0.48	93.5±0.98
CVF2	99.5 ± 0.18	2.3 ± 0.1	6.3 ± 0.08	3.4 ± 0.4	0.109 ± 0.01	3.2 ±0.34	99.2±0.97
CVF3	101.6 ± 0.16	2.6 ± 0.1	6.4 ± 0.06	3.6 ± 0.6	0.132 ± 0.01	4.2 ±0.42	95.9±0.85
CVF4	100.6 ± 0.22	2.4 ± 0.2	6.3 ± 0.07	4.2 ± 0.3	0.112 ± 0.01	4.4 ±0.53	94.8±1.02
CSF1	100.9 ± 0.20	2.3 ± 0.3	6.3 ± 0.10	3.5 ± 0.4	0.119 ± 0.01	3.4 ±0.47	97.5±0.96
CSF2	98.6 ± 0.22	2.2 ± 0.2	6.3± 0.09	4.3 ± 0.2	0.109 ± 0.01	4.5 ±0.58	98.1±1.04

All values represent Mean ± SD, n = 3

Table 4. Evaluation of the indomethacin sustained release tablets properties

Formulations	Avg. Wt. of Tablet (mg)	Thickness (mm)	Diameter (mm)	Hardness (kg/cm^2)	Friability (%)	Drug content %
SVF1	152.5 ± 0.25	4.0 ± 0.2	6.25 ± 0.12	5.6 ± 0.5	0.150 ± 0.008	97.57±0.987
SVF2	224.6 ± 0.18	5.0 ± 0.1	6.4 ± 0.08	6.3 ± 0.4	0.33 ± 0.012	92.72±0.978
SVF3	292.0 ± 0.16	5.0 ± 0.1	6.4 ± 0.06	6.8 ± 0.6	0.15 ± 0.011	90.90±0.856
SVF4	372.0 ± 0.22	5.5 ± 0.2	10.5 ± 0.07	5.8 ± 0.3	0.24 ± 0.014	101.2±1.026
SHF1	151.6 ± 0.20	4.4 ± 0.3	6.42 ± 0.10	5.7 ± 0.4	0.42 ± 0.014	95.75±0.961
SHF2	227.0 ± 0.22	4.9 ± 0.2	6.34 ± 0.09	6.8 ± 0.2	0.20 ± 0.015	98.77±1.042

All values represent Mean ± SD, n = 3

Table 5. Drug release mechanism of indomethacin conventional tablets

Formulations	Zero order R^2	First order R^2	Higuchi model R^2	Koresemeyer peppas model R^2
CVF1	0.959	0.964	0.990	0.897
CVF2	0.906	0.923	0.984	0.842
CVF3	0.975	0.979	0.970	0.930
CVF4	0.952	0.953	0.990	0.985
CSF1	0.959	0.966	0.991	0.894
CSF2	0.962	0.967	0.976	0.909
MARKETED PRODUCT	0.949	0.986	0.995	0.929

Table 6. Drug release mechanism of indomethacin sustained release tablets

Formulation	Zero order R^2	First order R^2	Higuchi model R^2	Koresemeyer peppas model R^2
SVF1	0.955	0.942	0.988	0.738
SVF2	0.997	0.992	0.948	0.934
SVF3	0.988	0.979	0.962	0.790
SVF4	0.988	0.982	0.960	0.750
SHF1	0.960	0.935	0.920	0.892
SHF2	0.976	0.956	0.989	0.749
MARKETED PRODUCT	0.947	0.970	0.992	0.791

Figure 1. The seeds of black gram

Figure 2. IR spectrum of indomethacin, *Vignal mungo* seed powder and physical mixture

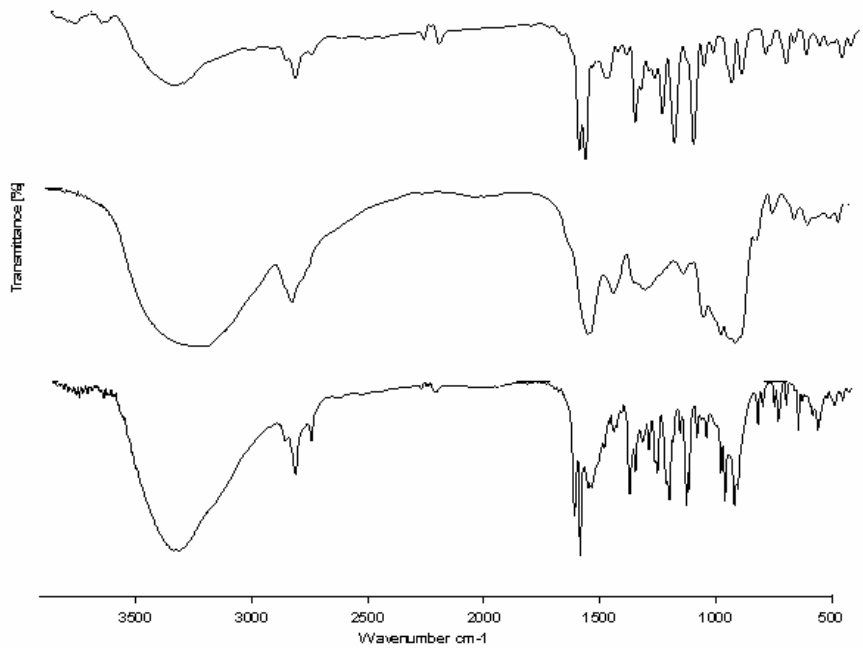


Figure 3. Dissolution profile of indomethacin conventional tablets

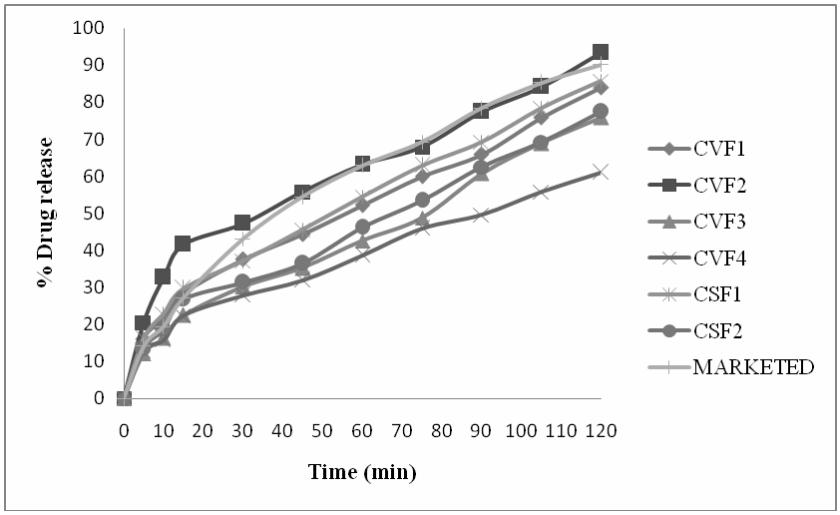


Figure 4. Dissolution profile of indomethacin sustaine release tablets

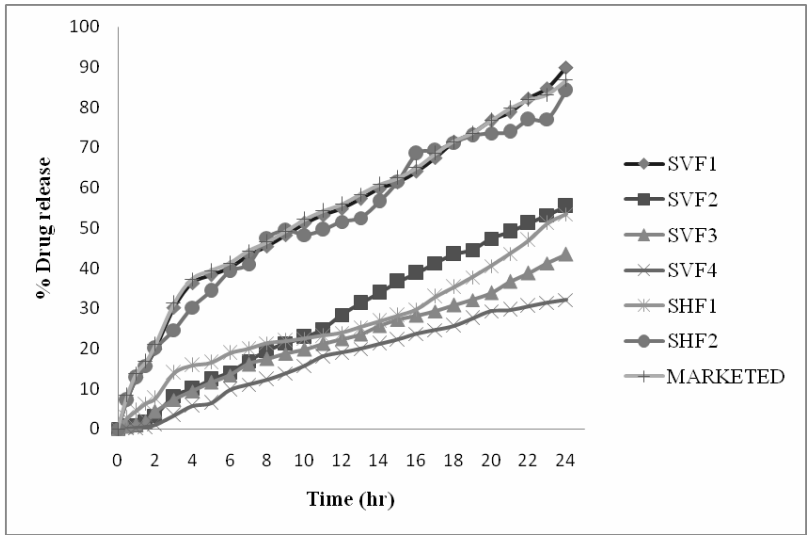


Figure 5. Swelling index of indomethacin sustained release tablets

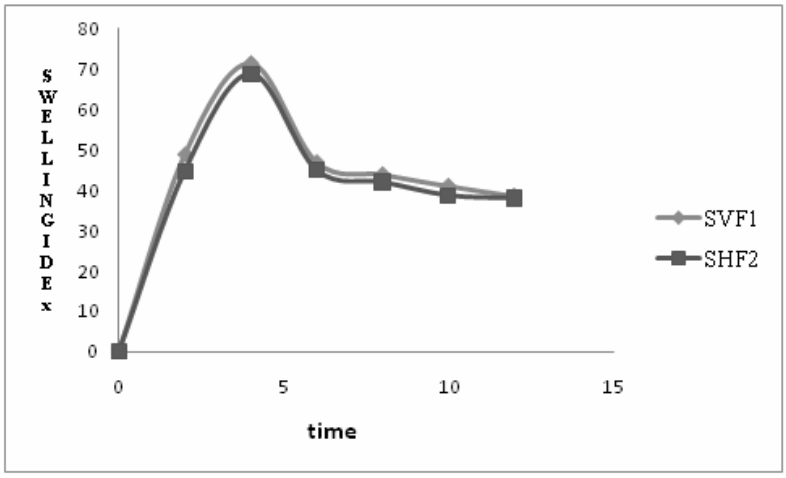
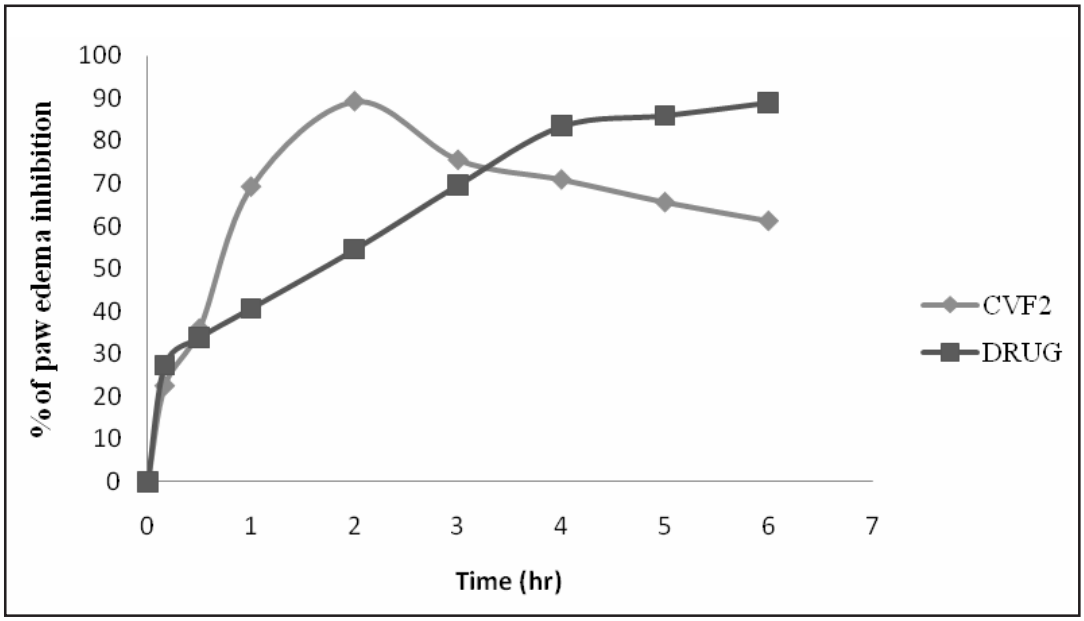


Figure 6. Anti-inflammatory activity of indomethacin and CVF2



All values represent Mean ± SD, n = 3

Reference

Bodempudi Sravani, R. and Bharath, B.V. (2011). Studies on *Vigna mungo* mucilage as a pharmaceuticl excipients. J. Chem. Pharm, Res., **3**(2):118-125.

Indranil Kumar Yadav; Durga Jaiswal; Niladry Ghosh; Hari Pratap Singh; Aushutosh Mishra; Arundhati Bhattacharya and Meenakshi Bajpai (2009). Evaluation of seed flour of *Vigna mungo* (L.) based sustained release matrix tablets of diclofenac sodium. J. Pharm. Res., **2**(5):834-838.

Indian Pharmacopoeia (1996). Govt. of India, Ministry of Health and Family Welfare, The Controller Of Publications, New Delhi, **2**:554-555.

Kathiresan, K.; Kiran, K. and Vijjin, P. (2010). Formulation and development of indomethacin sustained release tablets. IJPRIF, **2**(1):794-797.

Onyilagha, J.C.; Islam, S. and Ntamatungiro, S. (1982). Comparative phytochemistry of eleven species of Vigna. Phytochemistry, **21**(2): 1149-1151.

Peppas N, A. and Sahlin, J. J. (1989). A simple equation for the description of solute release. ii. Coupling of diffusion and relaxation, Int. J. Pharm., **57**:169-172.

Rang, H.P.; Dale, M.M.; Ritter, J.M. and More, P.K. (2003). Adverse reaction, clinical use of indomethacin, 5th edition of Pharmacology. pp. 245, 496, 719.

Sharma, J.N.; Samud, A.M. and Asmawi, M.Z. (2004). Comparison between plethysmometer and micrometer methods to measure acute paw edema for screening anti-inflammatory activity in mice. Inflammo Pharmacology, **12**(1):89-94.