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Original Article

Comparative evaluation of *Prosopis africana* seed gum as a sustained release binder in colon targeted diclofenac potassium floating tablets.

Salome A. Chime*, J.K. Okeke, G.C. Onunkwo

Department of Pharmaceutical Technology and Industrial Pharmacy, University of Nigeria, Nsukka 410001, Nigeria.

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Abstract

To formulate colon targeted diclofenac potassium floating tablets using a natural binder from *Prosopis africana* and compare with hydrophobic and hydrophilic binders. The tablets were formulated by direct compression using *Prosopis africana* gum (PAG), ethyl cellulose (EC) and sodium carboxy methylcellulose (SCMC) as binders and Eudragit L100 (EL100). The tablets were analysed for drug content, swelling index, buoyancy lag time (BLT) and total flotation time (TFT) among others. The properties of *Prosopis africana* gum and the tablets were studied using Fourier transform infra red spectroscopy (FTIR). The results of drug content of diclofenac potassium showed that they were within 90 -110 %. Tablets formulated with PAG all passed the disintegration time for sustained release tablets. Tablets formulated with PAG and EL100 had significantly higher BLT than those formulated without EL100 ($p < 0.05$). Tablets showed friability range of 0.49 to 2.08 % and also exhibited about 24 to 45 % drug release in simulated intestinal fluid pH 7.2 (SIF) at 8 h. All the major peaks of diclofenac potassium pure spectra were represented in the spectra of the tablets confirming there was no interaction between the drug and the polymer materials used. *Prosopis africana* gum could be used in formulating colon targeted diclofenac potassium floating tablets.

Keywords: Colon targeting, floating tablets, diclofenac potassium, *Prosopis africana*, sustained release.

1. Introduction

In recent years, plant derived polymers have evoked tremendous interest due to their diverse pharmaceutical applications such as diluents, binder, disintegrant in tablets, thickeners in oral liquids, protective colloids in suspensions, gelling agents in gels and bases in suppository. They are also used in cosmetics, textiles, paints and paper industry. These polymers such as natural gums and mucilage are biocompatible, cheap and easily available and are preferred to semi synthetic and synthetic excipients because of their lack of toxicity, low cost, availability, soothing action and non irritant nature. Furthermore, they can be modified to obtain tailor made materials for drug delivery systems allowing them to compete with the synthetic products that are commercially available. Many kinds of natural gums and mucilages are used in the food industry and for the formulation of drugs. These natural polymers are generally regarded as safe (GRAS) for human consumption [1].

Prosopis africana (mimosaceae) also called okpeye or ugba by the Igbos, and kiriya by the Hausa Nigeria and English (iron wood) is the only tropical African Prosopis species, occurring from Senegal to Ethiopia in the zone between the Sahel and savannah forests. Due to extensive overexploitation, it has

**Corresponding author.*
E-mail address: salome.chime@unn.edu.ng
(Salome A. Chime)

disappeared from extensive parts of the southern Sahel and the adjacent Sudan savannahs. It is a popular tree in Nigeria. The tree reaches 4-20 m in height; has an open crown and slightly rounded buttresses; bark is very dark, scaly, slash orange to reddish brown with white streaks [2-3]. The methanol stem bark extract has anti-inflammatory and analgesic properties. The tannins and dye in the bark is also utilized in the leather industry[4]. The leaves and stem are used for treating toothache. The fruits (pods) are used as fodder for ruminant animals [5]. In the middle belt states of Nigeria, fermented *Prosopis africana* seeds are popularly used as food seasoning. It is a source of low cost protein. Gels that could be used for pharmaceutical tablet formulation is obtained from Prosopis africana gum. The endocarp gum of Prosopis africana seed contains high content of galactose and mannose. Galactose is a special type of natural sugar that gives sustained energy for a longer time compared to other sugar. Mannose is important for treatment of urinary tract infections [6].

Prosopis gum is extracted from the seeds of *Prosopis africana* and has major monosaccharides components such as xylose and galactose. It also contains fructose and glucose to a lesser degree. The gum from the plant has been evaluated as suspending agents, binder, sustained release matrix and bio-adhesive in various dosage forms [7,8,9].

Presently our study is focused on the possible delivery of diclofenac potassium, a drug mainly used in geriatric patients in the treatment of pain and inflammation to the colon in the form of floating tablets in order to avoid the gastric irritation often encountered with the use of this drug.

Materials and methods

Diclofenac potassium (Healthy Life Pharma, India), *Prosopis africana* gum (locally extracted), distilled water (STC University of Nigeria Nsukka, Nigeria), ethyl cellulose, sodium carboxy methylcellulose, acetone, talc, sodium hydroxide pellets, monobasic potassium phosphate, citric acid, hydrochloric acid and sodium chloride (BDH, Poole, England); Eudragit L100 (Evonik, USA), sodium bicarbonate and magnesium stearate (Qualikems, India); and microcrystalline cellulose (Avicel PH 101-FMC Biopolymer corporation, USA).

Extraction of *Prosopis africana* gum

The *Prosopis africana* seeds were purchased from Orba market of Nsukka, Enugu State, Nigeria in the month of May, 2013 and authenticated by Mr. A.O. Ozioko, a consultant taxonomist with the International Center for Ethnomedicine and Drug Development (Inter CEDD) Nsukka. The seeds were washed and boiled for 8 h. The brown husk and the whitish embryo were removed from the seed leaving the whitish sticky substance. The whitish sticky substance was left to stand for 1 h in a bowel of water containing 0.1 % of sodium metabisulphite, to allow a complete extraction of the gum into the water [8]. This was pressed vigorously through a sieve for a thorough collection of the mucilage. The gum was later filtered to remove the dirt and foreign matter using muslin cloth bag, precipitated with acetone, filtered, dried in in a tray dryer (Manesty Ltd, Liverpool, England) at 40 ^{o}C and milled in an end runner mill (Pascal Engineering Co Ltd, England) and finally passed through 55 mm sieve (Turgens & Co., Germany).

Characterization of *Prosopis africana* gum

Solubility

The solubility of *Prosopis africana* gum was tested in methanol, ethanol, isopropyl alcohol, acetone and water. This process was carried out by shaken 50 mg of powdered *Prosopis africana* gum vigorously in a 250 ml beaker containing 50 ml of the solvents mentioned above.

Swelling properties

A 10 mg quantity of *Prosopis africana* gum was added into a calibrated pipette blocked at one end. A measured volume of distilled water was added to the gum and allowed to stand for 60 min. The swelling level of the granule in the pipette was recorded. Percentage swelling was calculated from equation below:

$$\% \text{ Swelling Index} = \frac{\text{Final Granule level - Initial Granule level}}{\text{Initial Granule level}} \times 100 \quad \text{——— 1}$$

Loss on dry (LOD)

The LOD method [10] was used to determine the inherent moisture content of the dry mucilage. A 1 g sample of the mucilage was heated at 105 ± 2°C to a constant weight in a microwave oven and the percent loss of moisture on drying was determined using the formula:

$$\text{LOD } \% = \frac{\text{Weight of water in mucilage}}{\text{weight of dry sample}} \text{ x } 100 \quad (2)$$

Pre compression tests

Angle of repose

The angle of repose of each batch of the powder mix was determined by the static method using the fixed base cone [11], and calculated using the equation:

$$\text{Tan } \theta = \frac{h}{r} \quad (3)$$

where h and r are the height and radius of the powder cone.

Compressibility index and Hausner's ratio

To calculate the Carr's compressibility index, both bulk density (BD) and tapped density (TD) were determined as previously described [11]. A 10 g quantity of each batch, previously shaken to break any agglomerate, was introduced into a 25 ml measuring cylinder. After the initial volume was observed, the cylinder was allowed to fall under its own weight onto a hard surface from the height of 2.5 cm at 2 sec intervals. The tapping was continued until no further change in volume was noted. BD and TD were calculated and used to calculate the Carr's indices and Hausner's ratio.

The compressibility index of each sample was determined using the equation [11]:

$$\text{Carr's Index (\%)} = \frac{[(TD-BD) \text{ X } 100]}{TD} \quad \text{---------- 4}$$

Hausner's ratio was calculated using the formula:

$$\text{Hausner's ratio} = \frac{TD}{BD} \quad (5)$$

Preparation of Diclofenac potassium floating tablet

All the concepts and assumptions of biopharmaceutics, i.e. absorption, distribution, metabolism and excretion, are the important factors for mathematical design of the sustained release dosage forms [12]. Based on this, the required dose of diclofenac potassium to achieve daily sustained blood level was calculated. Pharmacokinetic studies showed that a dose of 25 mg of diclofenac potassium produces an effective blood level concentration of 0.7 – 1.5 µg/ml within 1.5 – 2.5 h with the half life of 1.1 – 4.0 h.

Thus elimination rate constant,

$$K = \frac{0.693}{t_{1/2}} \quad (6)$$

$0.693/4 = 0.1732\ mg/h$. Hence the availability rate R = k x D (7)

0.1732 x 25 = 4.3 mg/h, where D is the usual dose of the drug.

The maintenance dose D_m = R X h (8)

i.e. 4.3 x 20 = 86 mg, where h is the number of hours for which sustained action is desired.

Thus, total dose = D + D_m (9)

25 + 86 = 111 mg

$D_{corrected}$ = D – Rtp (10)

25 – (4.3 x 2) = 164 mg, where t_p is the time period required to achieve a peak plasma level.

Therefore, total $dose_{corrected}$ = $D_{corrected}$ + D_m (11)

= 16.4 + 86 = 102.4 mg.

The tablets were produced by direct compression using the ingredients presented in Table 1. Sodium bicarbonate (20 %) and citric acid (5 %) were used in order to impart the formulations with floatation and effervescent capacities. Eudragit L100 (10%) was used in order to ensure the release of drug at pH of the colon. *Prosopis africana* gum, ethylcellulose and SCMC were used as binders respectively at concentrations 10 - 25 %. While talc and magnesium stearate were used as anti-adherent and lubricant

respectively. The tablets were compressed at 46-48 kg using a 9.0 mm punch and die set fitted into an automated F3 Manesty Single Punch tabletting machine.

Post compression tablet tests

Uniformity of Weight

The BP, 2009 method was employed in the weight uniformity test. Twenty tablets were randomly selected from each batch. The tablets were weighed together and individually using an electronic balance (Ohaus Adventurer, China) and the percentage deviations were determined thus:

$$\% \text{ deviation} = \frac{\text{Weight variation}}{\text{Actual weight of tablet}} \text{ x } 100 \qquad 12$$

Where, weight variation = weight of one tablet – mean tablet weight

Tablet friability test

Friability test was determined using a friabilator (Erweka GmbH, Germany) rotated at 25 rpm for 4 min as stipulated in BP, 2009 [10] . The tablets were weighed before and after rotation and the percentage friability calculated using:

$$\text{Friability} = 1 - \frac{W_f}{W_o} \text{ x } 100 \qquad (13)$$

where W_o and W_f are the initial and final weights of the tablets respectively.

Buoyancy lag time/Total floating time

Buoyancy studies were performed for all the tablet formulations. Tablets were randomly selected and dropped in a 100 ml beaker containing simulated gastric fluid (SGF) pH 1.2. The time taken for the tablet to rise to the surface and float which is the buoyancy lag time (BLT) or floating lag time (FLT) was recorded. The duration of time the dosage form constantly remained on the surface of medium was determined as the total floating time (TFT).

Swelling Index

The swelling index of the tablets was determined in both SGF pH 1.2 and simulated intestinal fluid (SIF) pH 7.2 separately at 37 ± 0.5 $^{\circ}$C. Tablets were selected randomly from each of the batches and placed in a basket in a 250 ml beaker containing 100 ml of the medium. At 0.5, 1, 2, 3, 4, 5, and 6 h each basket was removed from the medium and the tablet was blotted with tissue paper to remove the excess water and weighed with the analytical balance (Adventurer, Ohaus, China). The percentage swelling index of the floating tablet was calculated using the formula:

$$\% \text{ swelling index} = \frac{\text{final weight} - \text{initial weight}}{\text{initial weight}} \times 100 \qquad 14$$

FTIR spectroscopy

Fourier transform infra-red spectroscopic analysis (FTIR) of pure drug, polymers including PAG and tablets were obtained using a Shimadzu FTIR 8400 Spectrophotometer. The pellets were prepared on KBr press under hydraulic pressure of 150 kg /cm^2. The spectra were scanned over the wave number range of 4000-400 cm^{-1} at an ambient temperature.

Determination of hardness

Ten tablets form each batch was tested for the diametrical crushing strength using Monsanto hardness tester. The crushing strengths (hardness values) were determined (kgf) and compared with official specification [10].

Disintegration time test

The disintegration times of the tablets were determined in SIF (pH 1.2) maintained at 37.0 ± 1.0 ^{o}C using the disintegration tester (Erweka ZT 120 basket and rack assembly). Six tablets were selected at random from each batch and the machine operated until all the tablets disintegrated.

Drug content analysis

Twenty tablets were selected at random and carefully pulverized using mortar and pestle. An amount of the resulting powder equivalent to 100 mg of diclofenac potassium was accurately weighed, dissolved in 20 ml of water in 100 ml volumetric flask and made up to volume with water. Thereafter, the mixture was filtered using Whatman no 1 filter paper and the resulting filtrate was diluted appropriately and the absorbance readings was determined using a spectrophotometer (Jenway 6305, UK) at predetermined wavelength of 298 nm. The concentration of

drug was calculated with reference to Beer-Lamberts plot for diclofenac potassium.

Dissolution test

Tablet dissolution test was carried out using the USP XXIII basket method (Erweka Germany Type: DT 600) operated at 100 r/min for 8 h in 900 ml of simulated intestinal fluid pH 7.2 maintained at 37±0.5°C (United States Pharmacopoeia, 2004). At 0.25, 0.5, 0.75, 1, 2, 3, 4, 5, 6, 7, and 8 h time intervals, 5 ml of dissolution fluid was withdrawn and replaced with an equal amount of fresh prepared 0.1N HCl dissolution medium. Each withdrawn sample was filtered and the amount of drug released was determined using the UV-Visible spectrophotometer (Jenway 6305, UK), at 300 nm and concentration calculated with reference to Beer-Lamberts plot.

Kinetic analysis of *in vitro* release profiles

The dissolution data from the various batches were analysed to determine the *in vitro* release kinetic mechanism. Three kinetic models: the first order equation, Higuchi square root equation and Korsmeyer-Peppas empirical model were applied to the release data to find the equation with the best fit.

$$Q = 100(1 - e^{-K_1 t}), \quad (15)$$

$$Q = K_2 (t)^{1/2}, \quad (16)$$

$$M_t/M_\infty = K_3 t^n \quad (17)$$

where Q is the release percentage at time, t and K_1, K_2 and K_3 are the rate constants of first-order, Higuchi and Korsmeyer-Peppas models, respectively [13-15]. M_t/M_∞ is fraction of drug released at time t, n is diffusion exponent and is indicator of the mechanism of transport of drug through the polymer, k is kinetic constant (having units of t^{-n}) incorporating structural and geometric characteristics of the delivery system. The release exponent n = 0.5 and 1.0 for Fickian and non-Fickian diffusion from slab, respectively [13-16].

Statistical analysis

Data were analysed by one-way ANOVA. Differences between means were assessed by a two-tailed student's T-test. $P < 0.05$ was considered statistically significant.

Results and Discussion

Physical properties of *Prosopis africana* gum

The results of the physical properties of PAG showed that the yield was low (0.24 %). The mucilage showed a high swelling index of 87.8 % and low amount of moisture. The gum was soluble in water and insoluble in methanol, ethanol, isopropyl alcohol and acetone.

Flow characteristics

The results of angle of repose are shown in Table 2, and show that they were significantly below 40 ^{o} ($p < 0.05$). Batches D11 and D12 containing SCMC alone had significantly lower angle of repose values than the formulations containing PAG alone or in combination of other polymers. Hausner's quotient ranged from 0.75 to 0.88 indicating poor flowability, while Carr's compressibility index ranged from 12.5 to 25 %, indicating that the powder had fair flowability.

Tablets properties

Tablets weight uniformity and drug content

The results of tablets weight uniformity are shown in Table 3 and show that the tablets all passed the tests with percentage deviations significantly lower than 5 % as stipulated in the BP. The results of drug content of diclofenac potassium are shown in Table 3 and show that drug content lied within 90 -110 % as stipulated in the BP [10].

Disintegration time

The results of the disintegration time of tablets in SIF are shown in Table 3 and show that disintegration time ranged from 21.2 ± 0.68 to 23.3 ± 0.65 min for batches D2 and D1 formulated with PAG 20, and 10 % respectively and 10 % EL100, while batches D3 and D4 formulated with EC 10 and 20 % and 10 % EL100 had disintegration time of 64 ± 0.88 and 60.2± 1.84 min respectively. However, batches D5 and D6 formulated with SCMC 10 and 20 % and 10 % EL100 had

disintegration time of 123 ± 1.44 and 130 ± 2.66 min. Therefore, batches D1, D2, D3, and D4 formulated with PAG or EC showed better properties for the colon delivery of diclofenac potassium at concentrations used than those formulated with SCMC. However, diclofenac potassium tablets containing no EL100 (batches D7 to D12) all passed the disintegration time for sustained release tablets in SIF with disintegration time range less or equal to 60 min and exhibited significantly lower disintegration times than the EL100 containing tablets ($p < 0.05$). The results showed that PAG could be used alone or in combination with EL100 in formulating colon targeted diclofenac potassium.

Hardness and friability

The results of tablets hardness are also shown in Table 3 and show that diclofenac potassium tablets formulated with PAM 10 and 15 % (D1, and D2) exhibited harness of 11.42 ± 0.14 and 6.42 ± 0.11 Kgf, while those formulated with SCMC had hardness of 11.6 ± 0.38 and 10.54 ± 0.22 kgf respectively (D5 and D6). The results showed that all the batches exhibited hardness that is sufficient enough to ensure that the integrity of the tablets is not compromised.

The results of tablets friability tests are shown in Table three and show that the tablets all showed friability range of 0.49 to 2.08 % for tablets formulated with PAG alone or in combination with EL100 (batches D1, D2, D7 – D10). The results showed that tablets formulated with EC and SCMC had friability and hardness comparable to those formulated with PAG.

Buoyancy lag time and TFT

The results of the BLT are shown in Table 3 and show that diclofenac tablets formulated with PAG and EL100 had significantly higher BLT than those formulated without EL100 ($p < 0.05$). Batches D1 and D2 (PAG and EL100) had BLT of 300 min, while D3 and D4 (EC and EL100) had 130 and 138 min respectively. However, batches D5 and D6 formulated with 15 and 20 % of SCMC and 10 % of EL100, had BLT of 38 and 43 min respectively.

The results of TFT of the tablets are also shown in Table 3 and show that all the tablets formulated with both synthetic and PAG and containing EL100 had TFT of above 12 h (batches D1 – D6). Also batches D11 and D12 formulated with SCMC and no EL100 had TFT of above 12 h. However, batches D7-D10 formulated with 5, 10, 15 and 20 % of PAG and no EL100 had TFT range of 6 – 8 h.

Swelling index

The results of the swelling index of tablets samples formulated with hydrophilic (SCMS), hydrophobic (EC) synthetic polymers and a hydrophilic natural polymer (PAG) are shown in Fig. 1 and show that tablets formulated with PAG showed significantly higher ($p < 0.05$) swelling index than those formulated with EC. At 2 and 6 h batch D2 formulated with 20 % PAG had swelling index of 465.2 and 803 %, batch D4 (20 % EC and 10 % EL100) had 132.8 and 221.3 %, while batch D6 (20 % SCMC and 10 % EL100) exhibited 363 and 776.7 % swelling. The results showed that PAG exhibited good swelling properties alone and in combination with EL100.

***In vitro* drug release**

The results of the *in vitro* release of diclofenac potassium in SIF are shown in Fig. 2 and show that all the batches had good release. There was no burst effect in any of the formulations. At 0.5 h ($T_{0.5\ h}$) 14.2, 4.9, and 11.9 % of drug were released from batches D1 (15 % PAG and 10 % of EL100), D3 (15 % EC and 10 % of EL100) and D5 (15 % SCMC and 10 % of EL100) respectively. At $T_{4\ h}$, about 21.7, 20.5 and 23.7 % of drug were released from batches D1 (15 % PAG and 10 % of EL100), D3 (15 % EC and 10 % of EL100) and D5 (15 % SCMC and 10 % of EL100) respectively and at $T_{8\ h}$, about 24.3, 21 and 34.8 % of drug were released from batches D1 (15 % PAG and 10 % of EL100), D3 (15 % EC and 10 % of EL100) and D5 (15 % SCMC and 10 % of EL100) respectively. However, formulations containing no EL100 (batches D7-D11) had about 24 to 45 % drug release at 8 h. This showed that PAM could be used alone or in combination with some smart polymers like EL100 in order to target drugs to the colon because of this prolonged release effect.

***In vitro* release kinetics**

The results of the *in vitro* release kinetics of diclofenac potassium from tablets are shown in

Table 4. The results show that First order plot of log cumulative drug release versus time were linear (r^2 = 0.9 - 0.984) showing that drug release followed first order release. Higuchi plots were also linear (r^2 = 0.910 to 0.966). The Korsmeyer-Peppas mechanism was linear with n^2 range of 0.040 to 0.766.

FTIR Spectroscopy

The results of FTIR spectra of pure diclofenac potassium, PAG, Eudragit L100-55 and batch D2 containing PAG 20 % and Eudragit 10 % are shown in Figures 3, 4, 5 and 6. The results show that the major peaks on the Batch D2 containing PAG, Eudragit and diclofenac potassium occurs at 3500-3310 cm^{-1}, 2962-2853cm^{-1}, 1600-1500cm^{-1}, 1430-1350$cm^{-}1$, 1355-1260cm^{-1}, 1185-1167cm^{-1}, 1060-1030cm^{-1}, 742cm^{-1} and 500$cm^{-}1$. In Figure 4, it was observed that the major peaks in the pure spectra of *Prosopis africana* mucilage were represented in the spectra of batch D2 with the neglect of 2402cm^{-1} and 1631cm^{-1} stretches which were extremely weak. All the major peaks of diclofenac potassium pure spectra were represented in the batch D2 spectra confirming no interaction between the drug and the polymer materials used.

The flow properties was analyzed by using two different methods; direct method of flow under gravity and an indirect method that uses densification and packing geometry. Bulk and tapped densities (loose density) was used as indirect method of assessing flowability and results are shown in Table 2. The results of the loose densities were applied to flow indices to determine the flowability of the powder. The results showed that the powder exhibited flow capable of giving good tablets by direct compression. The results of Hausner's quotient indicated that the all the batches had good flowability as shown in Table 2. Hausner's ratio ≤ 1.25 indicates good flow, while > 1.25 indicates poor flow [11]. The results of angle of repose and Carr's index (11.8 to 25 %) showed that the formulations had fair flow capable of giving good tablets. Carr's index in the range of 5 – 16 indicates excellent flow, 12 – 16 shows good flow, 18 – 21 shows fair flow, 23 -35 show a poorly flowing powder that can be improved using glidants, while values above 38 shows very poor flow [11]. Flow properties of powder is important in tableting and capsule filling because it affects the weight of the tablets, drug content and bioavailability of the drug. The results of the disintegration time of tablets showed that the tablets formulated without EL100 (D7-D12) all complied with BP (2009) [10] specifications for tablets disintegration time of sustained release tablets in SIF. However, Diclofenac potassium tablets formulated with PAG and EL100 passed the tests while those formulated with EC and SCMC failed. This may be due to concentration of binder used. The results showed that PAG may be a weaker binder than EC and SCMC. The results of tablets weight uniformity showed that the tablets all were within the acceptable limits and this ensured for the uniformity in drug content. The results of the drug content revealed that the drug content were within the BP limits hence, was not affected by neither the excipient used nor the method of formulation. The results of tablets hardness and friability shown in Table 3 showed that tablets formulated with PAG all passed the tests. The results showed that the mechanical integrity of these tablets would not be compromised during packaging, transport and use. The results of the swelling shown in Table 3 and show that all the formulations had good swelling index, hence PAG could be used in formulating sustained release tablets because it had good swelling index comparable to that of EC and SCMC. The results of the BLT and TFT of the tablets shown in Table 3 showed that the tablets formulated with PAG had significantly higher ($p < 0.05$) BLT than those formulated with EC and SCMC. This showed that PAG is a good polymer for the formulation of floating tablets. The TFT also showed that the formulations had good floatation and hence these polymers could be used in formulating diclofenac potassium tablets with high gastric irritation tendency. The results of the *in vitro* drug release shown in Fig. 2 showed that the formulations had good sustained release properties. There was no burst effect seen in any of the formulations. Hence, PAG could be used alone or in combination of EL100 for the colon delivery of diclofenac potassium in order to avoid gastric irritation often encountered with the use of this drug.

The results of the *in vitro* release kinetics are shown in Table 4 and show that the release kinetics followed a mixed order. Higuchi and first order kinetics were predominant, hence the release mechanisms followed both diffusion and dissolution controlled process. The Korsmeyer-Peppas models showed that all the batches except batches D1 and D4 followed Fickian diffusion release mechanism ($n < 0.5$), however batches D1 and D4 followed non-Fickian release mechanisms i.e. diffusion and erosion may be implicated as mechanisms of drug release ($0.50 < n < 1.00$) [15-16]. The results of FTIR spectra of pure diclofenac potassium, *Prosopis africana* gum, Eudragit L100 and batch D2 containing *Prosopis africana* gum 20 % and Eudragit 10 % are shown in Figures 3-6 and show that the major peaks on the Batch D2 containing *Prosopis africana* gum, Eudragit and diclofenac potassium occured at 3500-3310cm^{-1} (N-H stretching vibration of amine), 2962-2853cm^{-1}(alkane C-H stretch), 1600-1500cm^{-1} (nitroso compound C-NO stretch), 1430-1350cm^{-}1(S-O stretch of sulfite group), 1355-1260cm^{-1} (O-H bending), 1185-1167cm^{-1} (sulfonyl compound S-O stretch), 1060-1030cm^{-1} (sulfonic acid S-O stretch), 742cm^{-1} (C-H alcoholic stretch) and 500cm^{-}1(C-X halogen stretch). The results showed that the chemical and molecular structure of diclofenac potassium were not altered or denatured by the excipients used. Hence PAG could be used in formulating this drug formulation.

Conclusion

Prosopis africana gum may be used alone or in combination with Eudragit L100 for the colon delivery of diclofenac potassium. The results showed that tablets formulated with EL100 were comparable to those formulated with EC and SCMC but exhibited significantly higher buoyancy lag time. The results also revealed that the tablets showed good mechanical properties and were not affected by this natural polymer as revealed by FTIR. The use of natural polymers in drug delivery is highly recommended as they are often made form edible sources therefore, the danger of being toxic to the body is eliminated compared with synthetic polymers used in drug delivery. Research into this field should also be continued in order to adequately study all its aspects.

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Table 1. Composition of diclofenac potassium floating tablets.

Batches / **Ingredient**	**D1**	**D2**	**D3**	**D4**	**D5**	**D6**	**D7**	**D8**	**D9**	**D10**	**D11**	**D12**
Diclofenac potassium (mg)	100	100	100	100	100	100	100	100	100	100	100	100
***Prosopis africana* gum (%)**	15	20	-	-	-	-	10	15	20	25	-	-
EC (%)	-	-	15	20	-	-	-	-	-	-	-	-
SCMC (%)	-	-	-	-	15	20	-	-	-	-	10	20
$NaHCO_3$ (%)	20	20	20	20	20	20	20	20	20	20	20	20
Eudragit L100 (%)	10	10	10	10	10	10	10	-	-	-	-	-
Citric acid (%)	5	5	5	5	5	5	5	5	5	5	5	5
Talc (%)	1	1	1	1	1	1	1	1	1	1	1	1
Mg stearate (%)	1	1	1	1	1	1	1	1	1	1	1	1
MCC q.s to (mg)	300	300	300	300	300	300	300	300	300	300	300	300

Note: EC-ethylcellulose; SCMC-sodium carboxy methylcellulose; $NaHCO_3$-sodium bicarbonate; Mg stearate-magnesium stearate; MCC-microcrystalline cellulose.

Table 2. Flow properties of diclofenac potassium powder blend.

Batches*	Bulk density (g/ml)	Tapped density (g/ml)	Hausner's quotient	Bulkiness $(g/ml)^{-1}$	Carr's index (%)	Angle of repose (^{o})
D1	0.531±0.06	0.6071±0.02	0.88	1.88	12.5	34.99±0.21
D2	0.531±0.09	0.6538±0.05	0.81	1.88	18.7	36.24±0.18
D3	0.5±0.00	0.6071±0.06	0.82	2.00	17.6	16.34±0.13
D4	0.5±0.01	0.6071±0.03	0.82	2.00	17.6	25.93±0.25
D5	0.531±0.02	0.6538±0.08	0.81	1.88	18.8	30.96±0.19
D6	0.531±0.02	0.6071±0.06	0.88	1.88	12.5	19.177±0.2
D7	0.425±0.04	0.5667±0.03	0.75	2.35	25.0	22.06±0.18
D8	0.425±0.07	0.5667±0.07	0.75	2.35	25.0	27.82±0.24
D9	0.472±0.04	0.5667±0.08	0.83	2.12	16.7	30.83±0.26
D10	0.5±0.00	0.5667±0.05	0.88	2.00	11.8	24.3±0.17
D11	0.405±0.05	0.5±0.00	0.81	2.47	19.0	18.92±0.27
D12	0.425±0.06	0.531±0.08	0.80	2.35	20.0	19.44±0.15

***D1-D2 (gum 15-20 %, Eudragit 10 %), D3-D4 (Ethylcellulose 15-20 %, Eudragit 10 %), D5-D6 (SCMC 15-20 %, Eudragit 10 %), D7-D10 (gum 10, 15, 20, 25 % respectively and no Eudragit), D11-D12 (SCMC 10-20 % only).**

Table 3. Post compression tablet test of diclofenac potassium.

Batch	BLT (min)ǂ	TFT (h)ǂǂ	Disintegration time ǂ (min)	Hardness ǂ (kgF)	Friability (%)*	Tablet weight (mg)*	DC ǂ (mg)
D1	300	≥ 12	23.3 ± 0.65	11.42±0.14	1.02	300 ± 0.42	103.5
D2	300	≥ 12	21.2 ± 0.68	6.42±0.11	0.99	299 ± 0.56	102.1
D3	130	≥ 12	64 ± 0.88	9.24±0.12	0.68	298 ± 0.39	96.5
D4	138	≥ 12	60.2± 1.84	10.12±0.31	0.85	298 ± 0.64	102.8
D5	38	≥ 12	123 ± 1.44	11.6±0.38	0.56	298 ± 0.61	99.3
D6	43	≥ 12	130 ± 2.66	10.54±0.22	0.51	298 ± 0.60	98.6
D7	60	8	6.33 ± 0.69	10.98±0.25	0.51	300±0.47	102.8
D8	80	7	5.83 ± 0.83	8.24±0.28	1.19	299±0.49	95.8
D9	60	6	12.3 ± 0.76	5.78±0.34	0.49	299±0.63	102.1
D10	83	6	6.33 ± 0.45	4.4±0.24	2.08	300±0.55	97.2
D11	70	≥ 12	49.7 ± 3.83	8.88±0.26	0.16	299±0.62	101.4
D12	84	≥ 12	61.7 ± 5.81	9.16±0.30	0.34	299±0.42	104.2

D1-D2 (*Prosopis africana* gum 15, 20 % and Eudragit 10 % each), D3-D4 (Ethylcellulose 15, 20 % and Eudragit 10 %), D5-D6 (SCMC 15, 20 % and Eudragit 10 % each), D7-D10 (*Prosopis africana* gum 10, 15, 20, 25 % resp.), D11-D12 (SCMC 10-20 % resp.), BLT-Buoyancy lag time, TFT-Total floating time, ǂ n = 6, * n = 20.

Table 4: *In vitro* release kinetics of diclofenac tablets.

Batches	First order	Higuchi	Ritger-Peppas	
	r^2	r^2	r^2	n
D1	0.900	0.910	0.979	0.766
D2	0.976	0.915	0.937	0.075
D3	0.902	0.952	0.991	0.051
D4	0.984	0.966	0.911	0.646
D5	0.931	0.934	0.941	0.323
D6	0.969	0.925	0.950	0.040
D7	0.969	0.910	0.932	0.113
D8	0.964	0.912	0.908	0.098
D9	0.934	0.925	0.937	0.126
D10	0.957	0.933	0.938	0.102
D11	0.997	0.958	0.903	0.207
D12	0.941	0.927	0.940	0.365

D1-D2 (*Prosopis africana* gum 15, 20 % and Eudragit 10 % each), D3-D4 (Ethylcellulose 15, 20 % and Eudragit 10 %), D5-D6 (SCMC 15, 20 % and Eudragit 10 % each), D7-D10 (*Prosopis africana* gum 10, 15, 20, 25 % resp.), D11-D12 (SCMC 10-20 % resp.)

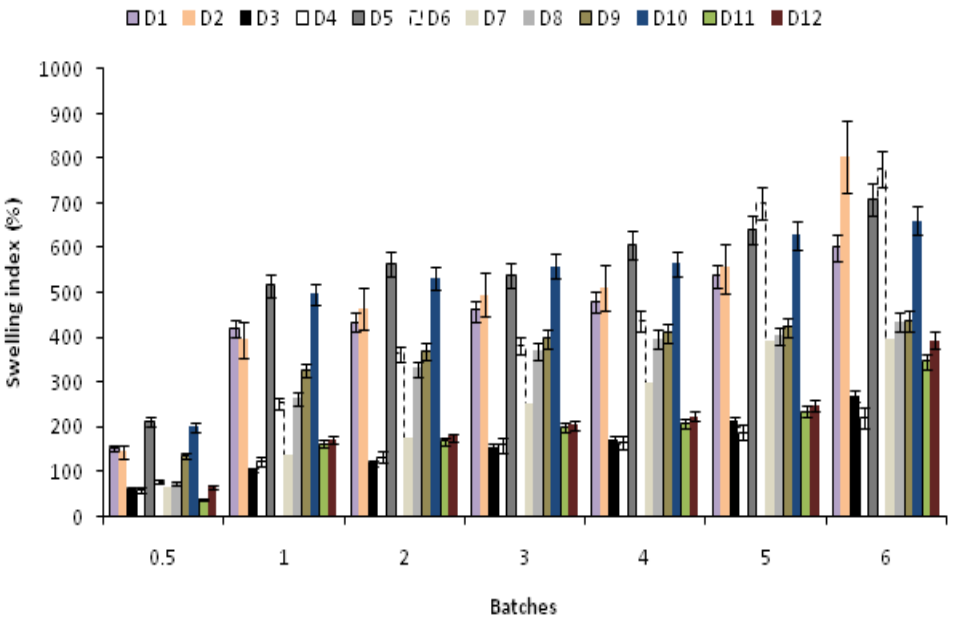


Fig. 1. Swelling properties of diclofenac potassium floating tablets.
D1-D2 (*Prosopis africana* gum 15, 20 % and Eudragit 10 % each), D3-D4 (Ethylcellulose 15, 20 % and Eudragit 10 %), D5-D6 (SCMC 15, 20 % and Eudragit 10 % each), D7-D10 (*Prosopis africana* gum 10, 15, 20, 25 % resp.), D11-D12 (SCMC 10-20 % resp.)

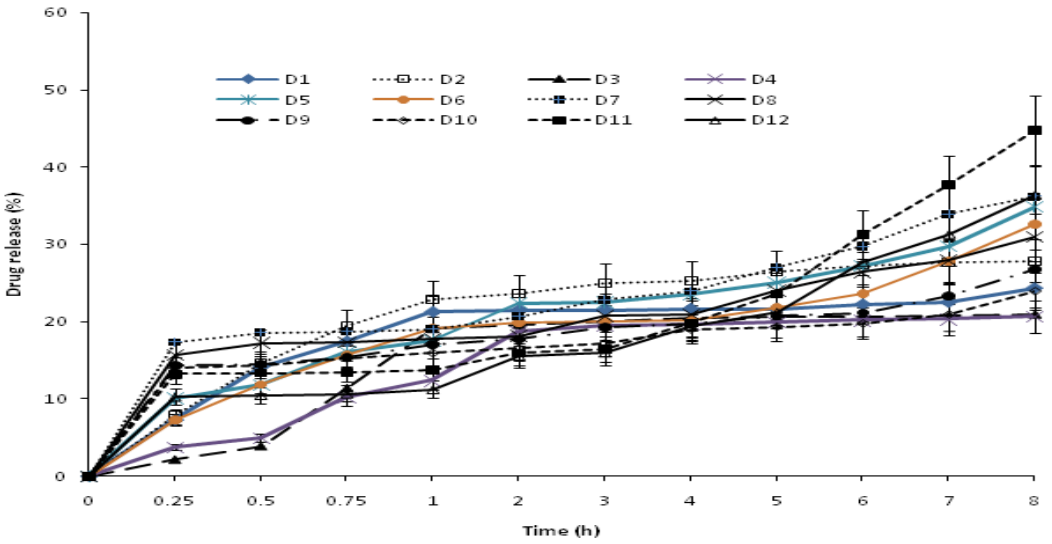
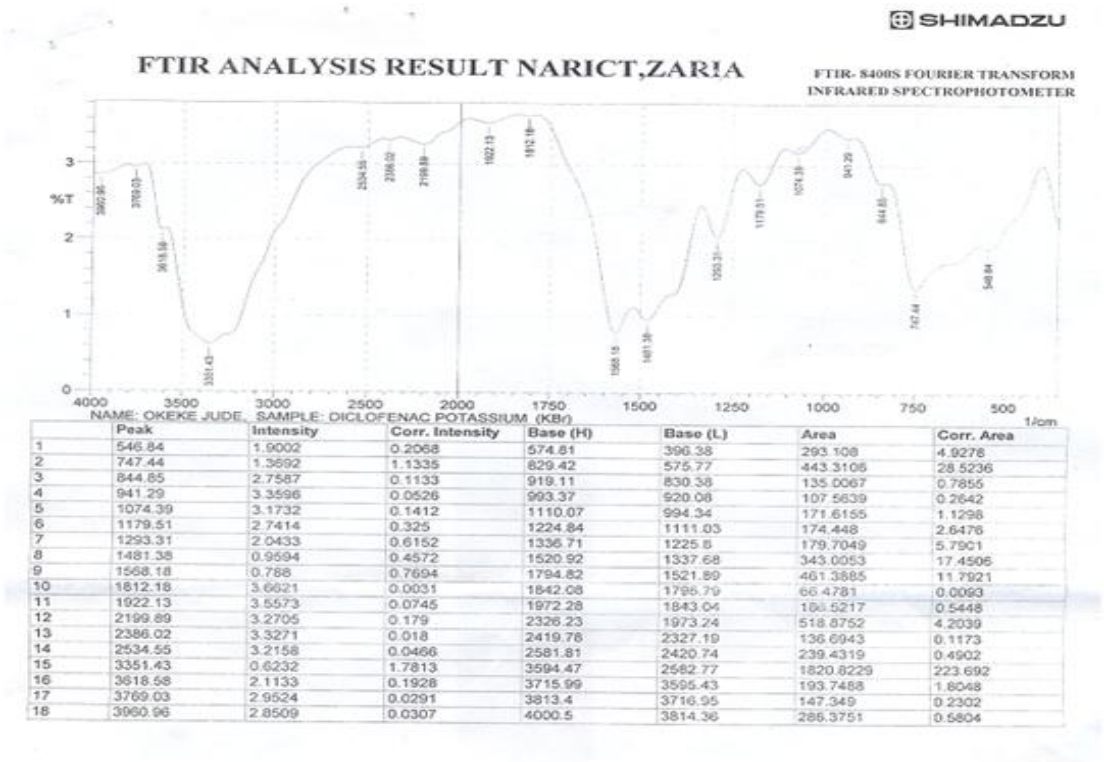


Fig. 2. *In vitro* release of diclofenac potassium from floating tablets in SIF (pH 7.2). D1-D2 (*Prosopis africana* gum 15, 20 % and Eudragit 10 % each), D3-D4 (Ethylcellulose 15, 20 % and Eudragit 10 %), D5-D6 (SCMC 15, 20 % and Eudragit 10 % each), D7-D10 (*Prosopis africana* gum 10, 15, 20, 25 % resp.), D11-D12 (SCMC 10-20 % resp.)

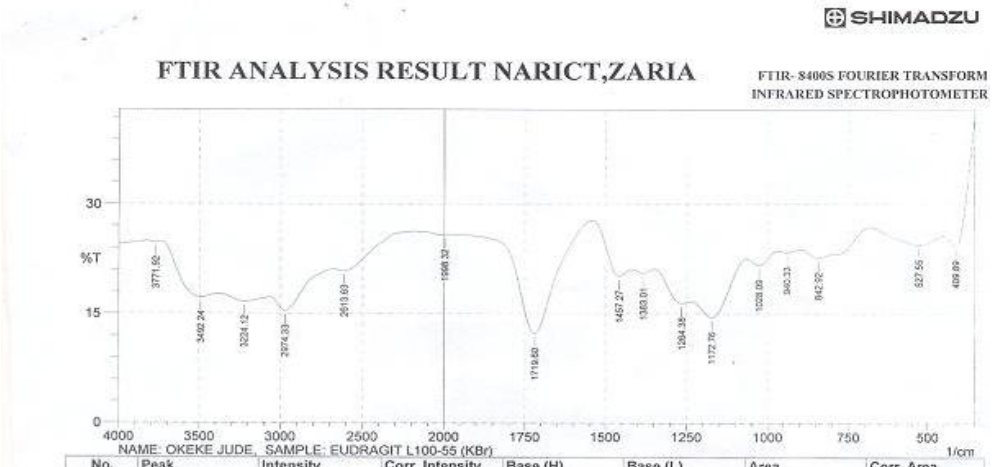


	Peak	Intensity	Corr. Intensity	Base (H)	Base (L)	Area	Corr. Area
1	546.84	1.9002	0.2068	574.81	396.38	293.108	4.9278
2	747.44	1.3592	1.1335	829.42	575.77	443.3105	28.5236
3	844.85	2.7587	0.1133	919.11	830.38	135.0067	0.7855
4	941.29	3.3596	0.0526	993.37	920.08	107.5639	0.2642
5	1074.39	3.1732	0.1412	1110.07	994.34	171.6155	1.1298
6	1179.51	2.7414	0.325	1224.84	1111.03	174.448	2.6476
7	1293.31	2.0433	0.6152	1336.71	1225.8	179.7049	5.7901
8	1481.38	0.9594	0.4572	1520.92	1337.68	343.0053	17.4506
9	1568.18	0.788	0.7694	1794.82	1521.89	461.3885	11.7921
10	1812.18	3.6621	0.0031	1842.08	1795.79	66.4781	0.0093
11	1922.13	3.5573	0.0745	1972.28	1843.04	186.5217	0.5448
12	2199.89	3.2705	0.179	2326.23	1973.24	518.8752	4.2039
13	2386.02	3.3271	0.018	2419.78	2327.19	136.6943	0.1173
14	2534.55	3.2158	0.0466	2581.81	2420.74	239.4319	0.4902
15	3351.43	0.6232	1.7813	3594.47	2582.77	1820.8229	223.692
16	3618.58	2.1133	0.1928	3715.99	3595.43	193.7488	1.8048
17	3769.03	2.9524	0.0291	3813.4	3716.95	147.349	0.2302
18	3960.96	2.8509	0.0307	4000.5	3814.36	286.3751	0.5804

Fig. 3. FTIR spectra of diclofenac potassium.

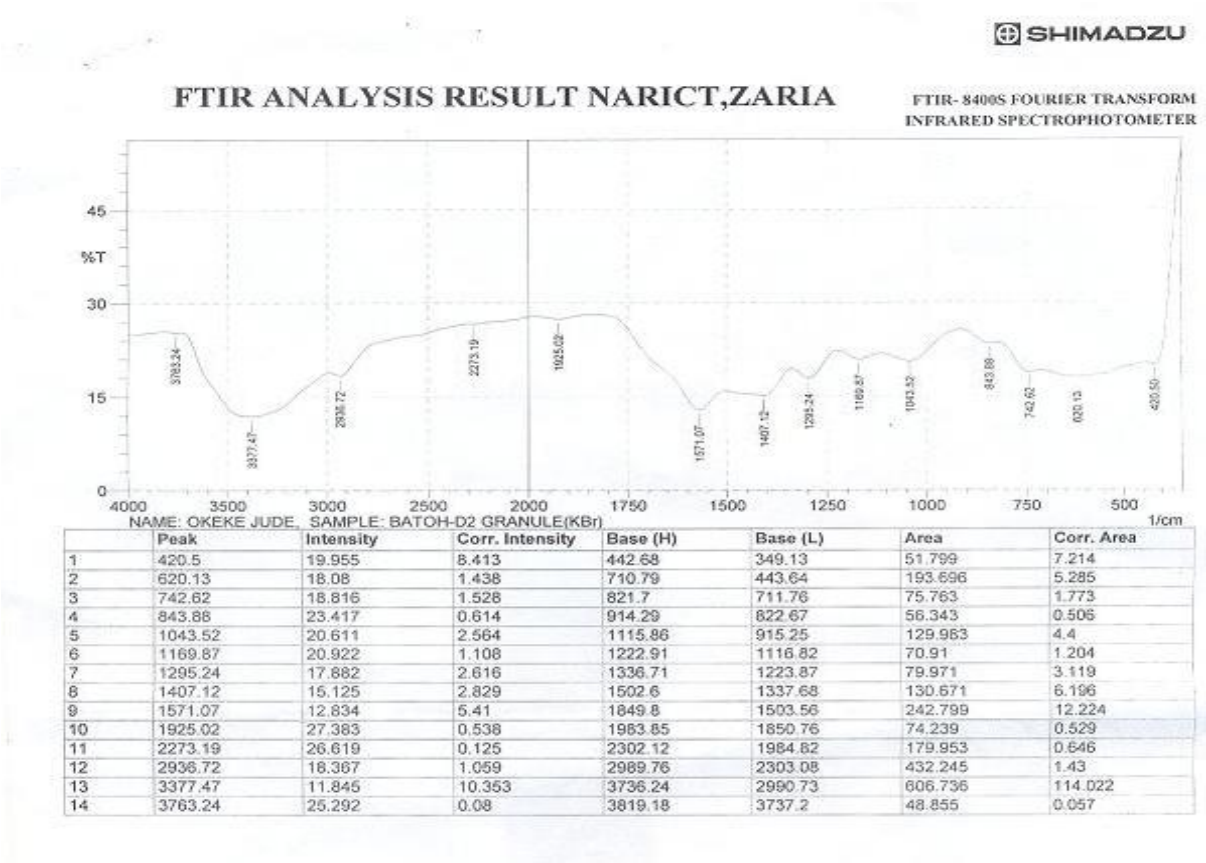
	Peak	Intensity	Corr. Intensity	Base (H)	Base (L)	Area	Corr. Area
1	411.82	20.745	7.35	451.36	349.13	62.155	7.026
2	477.4	21.7	0.191	535.26	452.32	54.818	0.135
3	587.34	21.650	0.269	654.49	536.23	207.186	1.110
4	1044.49	20.116	2.451	1220.02	655.46	243.094	7.578
5	1423.51	21.228	1.022	1520.92	1220.98	186.915	2.937
6	1831.83	21.362	0.978	1907.36	1521.89	188.377	2.594
7	2265.47	21.417	0.176	2314.68	1908.32	334.657	1.132
8	2402.42	21.009	0.075	2416.89	2315.62	68.189	0.114
9	2926.11	18.822	0.669	2999.41	2417.85	405.96	1.455
10	3411.22	16.159	3.052	3722.74	3000.37	545.931	28.661
11	3772.89	19.008	0.166	3822.09	3723.7	70.751	0.184
12	3983.14	18.708	0.046	4000.5	3823.04	128.52	0.267

Fig. 4. FTIR spectra of *Prosopis africana* gum.



No.	Peak	Intensity	Corr. Intensity	Base (H)	Base (L)	Area	Corr. Area
1	409.89	24.184	7.735	449.43	349.13	55.059	6.397
2	527.55	24.314	1.692	681.86	450.39	138.354	3.682
3	842.92	22.58	2.001	899.82	682.82	134.96	5.282
4	940.33	23.374	0.298	968.3	900.79	42.414	0.193
5	1028.09	21.633	1.305	1066.67	969.26	63.28	1.197
6	1027.13	14.483	4.378	1235.45	1067.64	128.142	8.674
7	1264.38	16.424	1.376	1347.32	1236.41	82.558	2.018
8	1383.01	20.528	0.576	1418.69	1348.29	48.002	0.434
9	1457.27	20.136	3.009	1542.14	1419.66	78.512	3.162
10	1719.6	12.276	14.634	1956.85	1543.1	276.108	39.118
11	1998.32	25.725	0.102	2182.53	1957.81	131.571	0.156
12	2613.63	20.83	0.908	2678.25	2183.49	310.462	2.563
13	2974.33	15.349	2.776	3066.92	2679.21	287.819	9.104
14	3224.12	16.646	0.822	3378.43	3067.88	238.678	3.328
15	3492.24	17.23	2.741	3736.24	3379.4	254.869	12.952
16	3771.92	24.717	0.137	3827.86	3737.2	54.902	0.108

Fig. 5. FTIR spectra of Eudragit L100.



	Peak	Intensity	Corr. Intensity	Base (H)	Base (L)	Area	Corr. Area
1	420.5	19.955	8.413	442.68	349.13	51.799	7.214
2	620.13	18.08	1.438	710.79	443.64	193.696	5.285
3	742.62	18.816	1.528	821.7	711.76	75.763	1.773
4	843.88	23.417	0.614	914.29	822.67	56.343	0.506
5	1043.52	20.611	2.564	1115.86	915.25	129.983	4.4
6	1169.87	20.922	1.108	1222.91	1116.82	70.91	1.204
7	1295.24	17.882	2.616	1336.71	1223.87	79.971	3.119
8	1407.12	15.125	2.829	1502.6	1337.68	130.671	6.196
9	1571.07	12.834	5.41	1849.8	1503.56	242.799	12.224
10	1925.02	27.383	0.538	1983.85	1850.76	74.239	0.529
11	2273.19	26.619	0.125	2302.12	1984.82	179.953	0.646
12	2936.72	18.367	1.059	2989.76	2303.08	432.245	1.43
13	3377.47	11.845	10.353	3736.24	2990.73	606.736	114.022
14	3763.24	25.292	0.08	3819.18	3737.2	48.855	0.057

Fig. 6: FTIR spectra of (batch D2) diclofenac potassium tablets.

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