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Formulation, Characterization and Evaluation of *Lepidium sativum* Gum as a Potent Excipient for Formulation of Film

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Abstract

Films were prepared (viz. LSF1, LSF2, LSF3, LSF4, LSF5, LSF6) using 5 to 30 w/w of mucilage of gum of *Lepidium sativum* with different proportions of plasticizers methyl paraben, glycerine. The films were casted on mercury plate. Films prepared with different proportion of gum and 0.2 % w/v methyl paraben, 2.5% w/v of glycerine showed satisfactory drying after 24 h. They were evaluated for qualitative phytochemical analysis followed by mechanical properties like water uptake, tensile strength, folding endurance, and water vapor transmission rate and stability studies also done for plane film. Further the gum was evaluated for release parameter with model drug diclofenac sodium (0.5 % w/w) with same composition of methyl paraben and glycerine.

Study found that the LSF4 film shows the best result among other batches of *Lepidium sativum*.

Keyword: *Lepidium sativum,* natural gum, film, sustained release drug delivery systems, diclofenac sodium.

Introduction

Polymers are widely used in medicinal products, from complex formulations to biopharmaceuticals in prescription drug delivery systems. Pharmaceutical coating materials are characterized by mechanical properties (Rowe RC et al., 1984; Nagarsenkar M and Hegde, 1999), permeability (Sun C., et al., 1999)., 1987) and water vapor transport (Shogren, R., 1997). The coating process and nature of the dosage form did not affect the properties of the free film (Sprockel O. L., et al., 1990). Item Natural polymers are of interest to their use in drug delivery due to their presence, compatibility and degradation in natural and physiological conditions (Item) (Deveswaran R., et al., 2009) It is widely used in natural resins, varnishes, sealants, bonding medium, waterproofing and so on. uses of natural products such as rosin (pinaceae), dammar resin, sandalwood resin, frankincense, and guaiac resin were evaluated.

This paper deals with the evaluation of a natural gum for its use in preparing films for application as drug delivery systems and coating agents. There are several reports about the successful use of natural gums in various pharmaceutical preparations. The gum in the present study is an extract from the berries of *Lepidium sativum.*

Material and method

Lepidium sativum seeds were collected from local habitat and got authenticate by botanist from agricultural college. methyl paraben, glycerine and other solvents were purchased from S.D. Fine Chemicals.

Extraction of gums from the seeds of *Lepidium sativum*

The mucilage of Lepidium sativum was extracted according to previously reported methods (Patel et al., 2007; Srinivas et al., 2003; Ravikumar et al., 2007). To powdered seed (100g), water (99ml) and chloroform (1ml) were added so as to obtain the aqueous extract of the powder. It was filtered through muslin cloth and the mucilaginous filtrate was collected. To this mucilaginous solution, acetone was added so as to precipitate the mucilage. The precipitated mucilage was collected and kept in freezer for 8 hours and then dried in a lyophilizer.

Qualitative Phytochemical Analysis

The isolated gum was subjected to various phytochemical tests (Kokate, C. K., 2000, Khandelwal, K. R. 2002, Bruneton, J., 1999, Jarald, E. E., et. al.,2007) as Test for Alkaloids as Dragendorff's test, Mayer's test, Hager's test, Wagner's test, Test for carbohydrates *Molisch test,* Fehlings test (detection of reducing sugars), Test for proteins and amino acids as Biuret's tests,Million's test, Ninhydrin test, Xanthoprotein test, Tests for Steroids such as Salkowski Reaction, Liebermann-Burchard Reaction, Libermann's reaction, Test for Tannins and Phenolic compounds *Test for flavanoids as Ammonia test, Shinoda's/Paw test*, *Test for saponins Foam test, Libermann-Burchard test*, Test for Gums and Mucilages, Test for sterols and or triterpenes.

The extracts were refluxed with alcoholic potassium hydroxide until the saponification was complete. The saponification mixture was diluted with distilled water and extracted with diethyl ether. The ethereal extract was evaporated and the unsaponifiable matter was subjected to following tests *Libermann-Burchard test,* Salkowski's reaction, Hesses reaction, Hersch's Sohn's reaction, Test for Glycosides *Borntrager's test, Keller-Killiani test,* Legal test. (Kokate, C. K., 2000, Khandelwal, K. R. 2002, Bruneton, J., 1999, Jarald, E. E., et. al.,2007)

Physical parameters of extracted gums

Organoleptic Evaluation:

The isolated mucilage was subjected for various organoleptic evaluations which included evaluation of colour, odour, shape, taste and special features like touch and texture (Lachman, L.et. al., 1981, Nadkarni, K. M., 2002., Sundaram, J., et. al., 2008,) The majority of information on the identification, purity and quality of the material can be drawn from these observations

Bulk density

Loose Bulk Density (LBD) and Tapped Bulk Density (TBD) were determined. A quantity of 2 g of powder from each formula, previously lightly shaken to break any agglomerates formed, was introduced into a 10 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 second intervals. The tapping was continued until no further change in volume was noted. LBD and TBD were calculated using the following formula (Harnby N., et., al., 1987, Indian Pharmacopoeia 2014,)

$$\text{LBD} = \text{Weight of the powder} / \text{Volume of the packing}$$

$$\text{TBD} = \text{Weight of the powder} / \text{Tapped volume of the packing}$$

Compressibility Index

The compressibility of the granules was determined by Carr's Compressibility Index.

$$\text{Carr's compressibility index (\%)} = [(\text{TBD}-\text{LBD}) \times 100] / \text{TBD}$$

Or it can be expressed as Carr's Index relates the poured density of the material to the tapped density and was calculated by using the following relationship: (Harnby N., et., al., 1987, Indian Pharmacopoeia 2014,)

$$\text{Carr's Index} = \frac{\text{Tapped density} - \text{Poured density} \times 100}{\text{Tapped density}}$$

Table 1: Relationship between % compressibility and flowability

Percent compressibility	Type of flow
5-15	Excellent
12-16	Good
18-21	Fare-passable
23-25	Poor
33-38	Very poor
>40	Extremely poor

Hausner's ratio

It is the ratio of tapped density to bulk density.(Indian Pharmacopoeia 2014,)

$$\text{Hausner's ratio} = \frac{\text{Tapped density}}{\text{bulk density}}$$

Table 2: Values of Hausner ratio and comment

Values	Comment
Less than 1.25	Good flow
Greater than 1.5	Poor flow
Between 1.25-1.5	Added glidant normally improves

Angle of Repose (θ)

This is the maximum angle possible between the surface of a pile of powder or granules and the horizontal plane.

The powders were allowed to flow through the funnel fixed to a stand at definite height (h). The angle of repose was then calculated by measuring the height and radius of the heap of granules formed. (Bagnold RA (1966), Indian Pharmacopoeia 2014,)

$$\text{Tan}\theta = h/r$$

$$\theta = \tan^{-1}(h/r)$$

Where, θ = angle of repose
h = height of the heap
r = radius of the heap

Table 3: The relationship between Angle of repose and powder flow

Angle of repose	Powder flow
< 25	Excellent
25-30	Good
30-40	Passable
> 40	Very poor

The lower the angle of repose, the better the flow properties, when granules are placed in the hopper & allowed to slide down into the die for compression. It forms a pile. The angle of

repose may be calculated by measuring the height (h) of the pile and the radius of the base (r)

with ruler. The angle of repose shows in between 30-40°C which is considered as passable flow of granules.

Loss on drying

10 grams of extracted gums was heated in a hot air oven (GallenKamp, England) at 105 °C. Loss on drying (LOD) was the difference between the initial weight and the final weight of the sample expressed as a percentage (Khandelwal, K. R. 2003, Indian Pharmacopoeia 2014.)

%LOD = initial weight-final weight / initial weight × 100

Solubility test

A 1.0 g of powdered gum was weighed and suspended in the respective solvents and was agitated for 24 h over a magnetic plate. A 1.0 ml from the supernatant was filtered and dried at 50° C. The gain in weight of previously tarred porcelain was taken as the amount of solute in the filtrate and this was used to calculate the solubility of the substance in 100 ml of the solvent. (Pujari, S. G., 1981, Indian Pharmacopoeia 2014,)

pH

The pH of 1% suspension was determined using digital pH meter 3310 (Genway) at 25°C. (Indian Pharmacopoeia 2014,)

Viscosity

Rheological studies of dried mucilage were carried out using concentration (1% w/v) prepared in distilled water. The viscosities were measured using an Oswald's viscometer (Indian Pharmacopoeia 2014).

Swelling index:

Swelling index of mucilage was determined by accurately weighed 1 g of mucilage powder was transferred into a 25ml glass Stoppard measuring cylinder. The initial bulk volume

was noted. Then 25ml of water was added and mixture was shaken thoroughly every 10 min for 1 h. It was then allowed to stand for 3h at room temperature. Then the volume occupied by mucilage, was measured. The same procedure was repeated thrice and the mean value was calculated. Swelling index (SI) is expressed as a percentage and calculated according to the following equation. (Khandelwal K. R., 2010.)

Swelling index (SI) =V_2-V_1V_1× 100

Where: V1is initial volume of powder before hydration.

V_2 is volume of swollen powder after (3 hours) hydration.

Ash values:

Ash values such as total ash, acid insoluble ash and water soluble ash were determined according to Indian Pharmacopoeia. The following procedures were used for determination of ash values. (Khandelwal, K. R. 2010.)

a) Total Ash:

About 3 g of sample was accurately weighed and taken in a silica crucible, which was previously ignited and weighed. The powder was spread as a fine, even layer on the bottom of the crucible. The crucible was incinerated gradually by increasing temperature to make it dull red hot until free from carbon. The crucible was cooled and weighed. The procedure was repeated to get constant weight. The percentage of total ash was calculated with reference to air dried sample. (Khandelwal, K. R. 2010.)

b) **Acid Insoluble Ash**: The ash obtained as described above was boiled with 25ml of 2N HCL for five minutes. The insoluble ash was collected on an ash less filter paper and washed with hot water. The insoluble ash was transferred into a silica crucible, ignited and weighed. The procedure was repeated to get a constant weight. The percentage of acid insoluble ash was calculated with reference to the air-dried sample. (Khandelwal, K. R. 2010.)

FTIR analysis

Pure drug sample, extracted mucilage and the physical mixture of drug with excipient in the ratio 1:1 were subjected to IR spectral studies using FTIR spectrophotometer (Zhang, Z., et. al.,2000). A physical mixture of drug and isolated mucilage was mixed with desirable quantity of potassium bromide. 100 mg of this mixture was compressed to form a transparent pellet using hydraulic press at 15 tons pressure. It was scanned from 4000-400 $^{cm-1}$ in a FTIR – 8400 Shimadzu, JAPAN (Jindal M,2013). The individual spectra of the drug and mucilage were performed.

Film casting evaluations for the extracted gum

The films were prepared on the mercury substrate by solvent casting method (Mundada A., et. Al., 2011) with extracted Cordia dichotoma gum. The plasticizer, glycerine, was added to 5 ml of distilled water and kept for stirring on a magnetic stirrer. To this solution, the weighed quantity of polymer was added and stirred till it gets dissolved completely. Then the weighed quantity of excipients like the methyl paraben was then added to the solution. In case of air entrapment, the air bubbles were removed by sonication (Oscar sonicator). The homogenous solution was then casted on a petri plate and dried at 40°C in hot air oven for 20 h (Mundada A., et. Al., 2011)

Evaluation of Mechanical properties of film

Thickness of the Film

The thickness of films was measured with the help of micrometer screw gauge at different strategic locations like four corners and centre of the each film. Mean SD is calculated. The standard range for film thickness should not be less than 5 %. This is essential to assure uniformity in the thickness of the film. (Mundada A., et. Al., 2011, Zhang, Z., et. al., 2000).

Folding Endurance

It is measured manually for the prepared film. A film was repeatedly folded at 180° at the same place till it breaks. This test was performed on three films of each formulation and mean ±SD was calculated. (Mundada A., et. Al., 2011, Zhang, Z., et. al., 2000).

Tensile strength

Tensile strength is the maximum stress applied to a point at which the film specimen breaks. Tensile strength of the optimized batch formulation was evaluated by a digital tensile strength tester. The test was carried out in triplicates and the average value was noted. (Mundada A., et. Al., 2011, Zhang, Z., et. al., 2000).

Water Uptake

The water uptake was determined by drying the films at 60°C with a current of air, after which the films were subjected to desiccation over calcium chloride at 40°C for 24 h. These samples were weighed and exposed to 70% relative humidity at room temperature. This relative humidity was achieved using saturated solutions of sodium chloride. After equilibration under this humidity, films were weighed for determining the increase in weight; and percent water uptake was calculated. (Mundada A., et. Al., 2011, Zhang, Z., et. al., 2000).

Determination of piercing load

The apparatus used for hardness determination was employed with a slight modification. The test was carried out by placing the film between two metal dies with an aperture diameter of 2 mm in both the dies. While the two dies hold the film in position, the increments of weights were added on to the wooden plate. The needle moves down across the film as and when the piercing load value is exceeded. The procedure was carried out on 5 films selected at random and the mean values for piercing load were recorded. (Jindal M, et. Al., 2013)

Surface pH

Film was soaked in 2 ml of distilled water for 15 min. Surface pH of films was determined using pH paper (Jindal M, et. Al., 2013).

Scanning Electron Microscopy

The Scanning Electron Microcopy (SEM) is used to identify the particle size and the surface morphology of the prepared films. The film is placed on the covered glass slide and then dried by applying vacuum, later it was coated with gold to a thickness of 100A using VEGAS TESCAN Vacuum evaporator and the image was captured for the prepared film.The surface topography of the prepared film were observed by optical microscopy using a calibrated eyepiece micrometer, and photographs were taken at ×400 magnification with a digital camera (Olympus, 8.1 megapixel, Japan). (Kalu V.D., et. al., 2007)

Stability Studies of Films

Stability test was conducted for 30 days at different temperatures: 4, 45 and 60 °C. At specific intervals of time (Day 5, 10, 15, 20, 25 and 30), films were taken out to assay their drug content, appearance and texture. (Kalu V.D., et. al., 2007, Sinha P, 2015.,)

Evaluation of Mechanical properties of drug loaded films containing extracted gum

The drug loaded films were evaluated as same for plane film of gum.

Study of in vitro Drug Release Kinetics

The in vitro diffusion data studies were analyzed for establishing kinetics of drug diffusion. The model fitting was done using an in-house program developed by Zero order (cumulative % drug release vs time), First order (log cumulative % drug remaining vs time), Higuchi (cumulative % drug release vs square root of time) and Peppas (log cumulative % drug release vs log time), were tested. Three different films formulations of three different herbal gum films were processed for the prediction of release profiles. Diclofenac sodium was used as the model drug. All above mentioned formulations were subjected for the mathematical modeling for the prediction of the release profiles. The relevant data on the film formation as well as diffusion of the active agents from the films has been fitted into various equations for the mathematical modeling. This modeling gives an overall idea on the drug release kinetics and possible mechanism of drug release characteristics. The drug release profile obtained from the In vitro release from various formulations was mathematically treated with various models to predict how a delivery system might function and gives valuable insight into its in vivo behavior. All the formulations were subjected to in vitro release studies. The results obtained of in vitro release studies were attempted to fit into various mathematical models available in the

software to fit the release studies. In this software various models such as Zero order kinetics (cumulative percentage amount of drug release versus time), First order kinetics (log cumulative percentage of drug remaining to release versus time), Higuchi (fraction of drug release, Mt/Mi, versus square root of time) and Peppas (log fraction of drug released, log Mt/Mi, versus log time) were applied to assess the kinetics of drug release from prepared films. Most suited model for drug release was predicted on the basis of regression coefficient i.e. nearer the value of regression coefficient towards 1, greater the suitability of best fitted release mechanism. (Nayak A. K., et. al., 2013, Nayak A. K., et. al., 2011, Sinha P, 2015.,)

RESULTS AND DISCUSSION

Various natural polymers have been investigated for their application as pharmaceutical adjuvants. Cordia gum is a biopolymer obtained from the plants and the present communication is an investigation of the physicochemical characteristics and film-forming properties of Cordia gum.

Extraction of gums from plant materials

Three selected plant gums were extracted from the seeds of Lepidium sativum. The percent yields of the plant gum were calculated. The calculated percent yield of 9.30 % for the extraction of *Lepidium sativum*gum (**Table 4**). The gum is initially white in color but changes to reddish brown to brownish black on exposure to air and temperature as it goes to dry. It is sparingly soluble in water but swells in contact with water, giving a highly viscous solution.

Table 4: Percent yield of gum extractions

Plant gums	***Lepidium sativum* gum**
Source plant parts	Seeds
% Yield	9.30 %

Phytochemical evaluation of the extracted gum

These extracted gum from *Lepidium sativum* was characterized for various important phytochemical qualitative tests.

Table 5: Phytochemical qualitative tests on extracted gums

Sl. No.	**Tests**	***Lepidium sativum* gum**
1	**Tests for Alkaloids:**	
	a)Dragendorff 's test	- ve
	b) Mayer’s	- ve
	c) Wagner’s	- ve
	d) Hager’s	- ve
2	**Tests for Glycosides:**	
	a)Keller - Killaine test	- ve
	b)Balget test	- ve
	c) Bromine water test	- ve
	d)Legal test	- ve
3	**Tests for Carbohydrates:**	
	a)Barfoed's test	+ ve
	b) Benedict’s test	+ ve
	c) Molisch’s test	+ ve
	Tests for Starches:	
	a) Iodine test	- ve
4	**Tests for Flavonoids:**	
	a)Shinoda test	- ve
	b) Alkaline reagent tests	- ve
	c) Ferric chloride test	- ve
	d) Lead acetate solution test	- ve
5	**Tests for Triterpenoids and Sterols:**	
	a)Liebermann – Burchard test	- ve

	b)Salkowaski test	- ve
7	**Tests for Saponins:**	
	a)Haemolysis test	- ve
	b) Foam test	- ve
8	**Tests for Proteins:**	
	a)Xanthoproteic test	+ ve
	b)Ninhydrine test	- ve
	c)Millon's test	+ ve
	d) Biuret test	- ve
9	**Tests for Tannins:**	
	a)Gelatin test	- ve
	b) Ferric chloride test	- ve

Physical parameters of extracted gums

The extracted plant derived *Lepidium sativum* gum was characterized for physical parameters like color, odor, taste, pH, Loss on drying (LOD), solubility, swelling index, viscosity, angle of repose, bulk and tap densities, Hausner's ratio, optical rotation, total and acid soluble ash values. The obtained results of various physical parameters of these three selected extracted gums are presented in **Table 6**.

Table 6: **Physical parameters of extracted gums**

Physical parameters	***Lepidium sativum* gum**
Colour	Buff colour
Odour	Characteristic
Taste	Mucilaginous
pH	6.3
LOD	9.40
Melting point	254-256°C
Solubility In water	Soluble
Solubility In organic solvent	Insoluble
Swelling index	NMT 7.9
Viscosity	347.2 cps
Angle of repose	14 °
Bulk density	0.7685 gram/ml
Tap density	0.9253 gram/ml
Hausner's ratio	1.2
Optical rotation (hydrolysed solution of 1 % w/v)	+ 1.78
Total ash value	7.6 w/v
Acid soluble ash values	1.06 % w/v

Characterization of extracted gums by Fourier Transform-infra Red (FTIR) spectroscopy analysis

The spectrum of extracted Lepidium sativum gum showed an identical broad band at 3696.56 cm−1 due to –OH stretching vibrations, peak at 2981.04 cm−1 due to C–H stretch, peak at 1454.27 cm−1 due to -C–H bend and peak at 1033.02 and 1011.52 cm−1 due to secondary –OH stretching (**Fig. 3**).

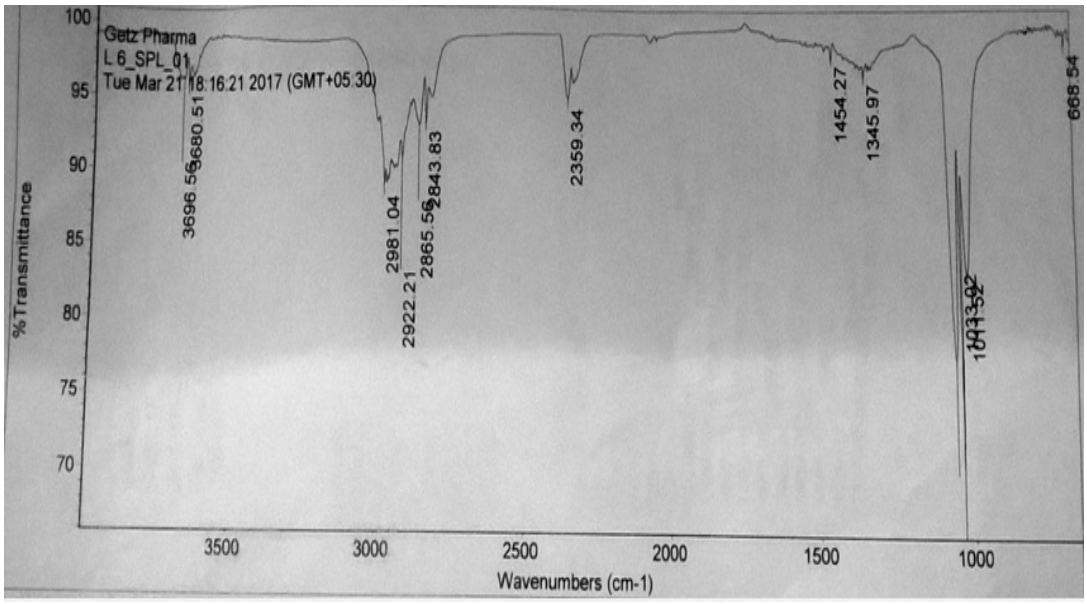


Fig. 1: FTIR spectrum of extracted *Lepidium sativum* gum

Film casting evaluations for the extracted gum

The prepared films made of extracted Lepidium sativum gum of 5-15 % w/w were found to have a dried appearance; whereas, films containing 30 % w/w of Lepidium sativum gum showed a wet appearance (Table 5.5). However, films containing Hibiscus esculentus gum of 20 and 25 % w/w (LSF4 and LSF5) revealed satisfactory appearances and accepted suitable for further evaluation. (**Table 7)**.

Table 7: Film casting ability of *Lepidium sativum* gum

Ingredients	Formulations					
	LSF1	LSF2	LSF3	LSF4	LSF5	LSF6
***Lepidium sativum* gum (% w/w)**	**05**	**10**	**15**	**20**	**25**	**30**
Glycerine (%w/v)	**2.5**	**2.5**	**2.5**	**2.5**	**2.5**	**2.5**
Methyl paraben (%w/v)	**0.2**	**0.2**	**0.2**	**0.2**	**0.2**	**0.2**
Appearance	**Dried**	**Dried**	**Dried**	**Satisfactory***	**Satisfactory***	**Wet**

Note: Satisfactory* means films which were suitable for further evaluation

Selection of the optimized films

The optimized films (drug free) made of *Lepidium sativum* gum were selected for further evaluations. The drug free films, which showed satisfactory film appearances, were selected as optimized films and were tested fatherly. LSF4 (containing extracted *Lepidium sativum* gum of 20 % w/w) were selected as optimized films for further evaluations.

Evaluation of mechanical properties of drug free films

The optimized film (drug free) containing extracted Lepidium sativum gum were evaluated for their mechanical properties like weight, mean thickness, folding endurance, water uptake, tensile strength, piercing load and surface pH. The weight of LSF4 was measured 208.76 ± 0.87 mg/cm2. The mean thicknesses of these optimized film was measured as 0.384 ± 0.140 mm for LSF4. Folding endurance of LSF4 weas determined as 251 ± 0.320. The water uptake by LSF4 film weas measured 7.38 ± 0.37 %. The tensile strengths of the film was calculated and 7.86 ± 0.36. The piercing load of film was computed as 0.254 ± 0.063 kg. The surface pHs of the film was measured and almost neutral pHs were measured. The surface pHs of LSF4 film was measured as 6.70 ± 0.05. The results of mechanical properties of drug free films containing extracted gums are presented in **Table 8**.

Table 8: Mechanical properties of drug free films containing extracted gums

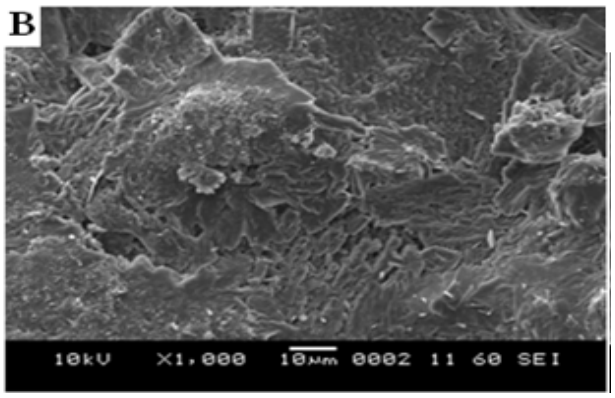
Films	Weight (mg/cm^2)	Mean thickness (mm)	Folding endurance (No. of folds)	Water uptake (%)	Tensile strength (kg/cm^2)	Piercing load (kg)	Surface pH
***Lepidium sativum* gum film**							
LSF4	208.76 ± 0.87	0.384 ± 0.140	251 ± 0.320	7.38 ± 0.37	7.86 ± 0.36	0.254 ± 0.063	6.70 ± 0.05

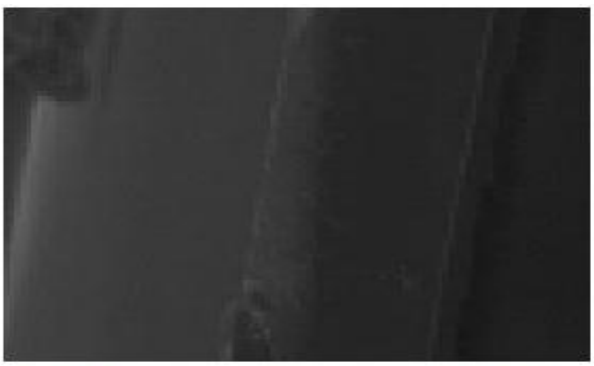
Mean ± S.E.; n = 3

Scanning electron microscopic (SEM) observation study

The optimized film (drug free) containing extracted Lepidium sativum gum was characterized morphological observation. The topography of LSF4 film presented in **Fig 2.** The cross-sectional morphology of the LSF4 film containing extracted Lepidium sativum gum in **Fig 3.**

Fig. 2 Topographical morphology LSF4 film (containing extracted Lepidium sativum gum) [B] by Scanning Electron Microscope





SEM cross sectional image of LSF4

Fig. 3: The cross-sectional morphology of LSF4 film (containing extracted Lepidium sativum gum) by Scanning Electron Microscope

Stability studies of drug free films

Stability testing was performed to reveal the stability of the optimized film (drug free) containing extracted *Lepidium sativum* gum (LSF4). The test was conducted for 30 days at different temperatures: 40, 45 and 60ºC. At specific intervals of time (Day 5, 10, 15, 20, 25 and 30), appearance and texture profiles of these drug free films was analyzed. The result of the stability study demonstrated absence of any significant changes in the appearances and textures. Therefore, the tested drug free film was found stable enough.

Identification of model drug for the formulation of solid dosage forms

Diclofenac sodium (a NSAID) is selected as model drug for the formulation of solid dosage forms. The physical nature, colour, melting point, and solubility of diclofenac sodium were determined and assessed (**Table 9**). Diclofenac sodium powder was found crystalline and of highly hygroscopic in nature. The colour of it was white to slightly yellowish. The melting point of diclofenac sodium was measured as 280 ± 0.5ºC. Diclofenac sodium was found soluble in ethanol and methanol. However, it was found sparingly soluble in water.

Table 9: Physical description of diclofenac sodium

Parameters	Descriptions
Nature	Crystalline powder; slightly hygroscopic
Colour	White to slightly yellowish
Melting point	280±0.5ºC.
Solubility	Soluble in ethanol and methanol, sparingly soluble in water

Diclofenac sodium was scanned for UV absorption with phosphate buffer pH 7.4 using a UV-VIS spectrophotometer and λmax value was determined. The λmax value of diclofenac sodium in phosphate buffer pH 7.4 was found 276 nm (**Fig. 4**).

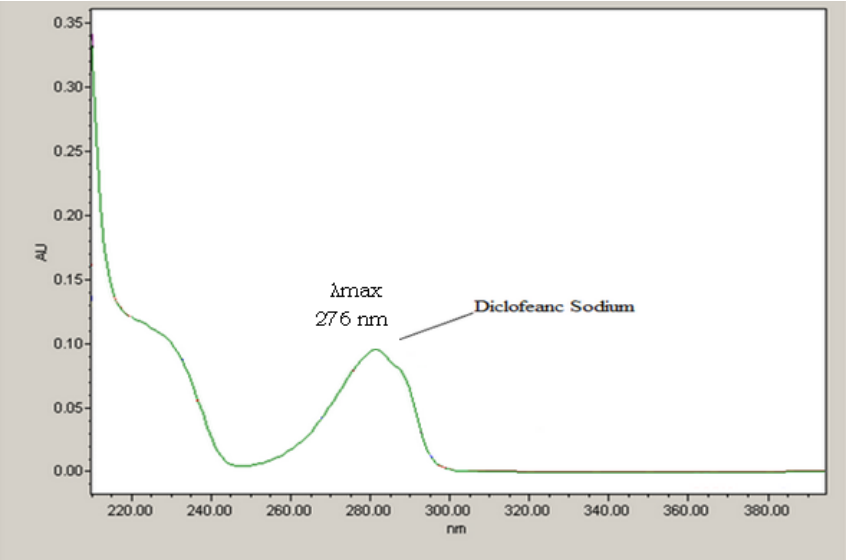


Fig. 4: Identification of diclofenac sodium by UV absorption

Diclofenac sodium was also identified by Fourier Transform-Infra Red (FTIR) spectroscopy analysis. The FTIR spectrum of diclofenac sodium is presented in **Fig. 5**. The FTIR spectrum of diclofenac sodium showed that the principal peaks at 1221.56 and 1318.68 cm^{-1} resulted from C-N stretching; whereas at 1517.56 cm^{-1} and 1603.34 cm^{-1} resulted from C=C stretching and C=O stretching of carboxyl group, respectively. The results of FTIR spectroscopy analyses were matched with the results of some previous studies (Nayak and Pal, 2011; Nayak et al., 2013; Sinha et al., 2015) and suggested that the tested sample can be diclofenac sodium.

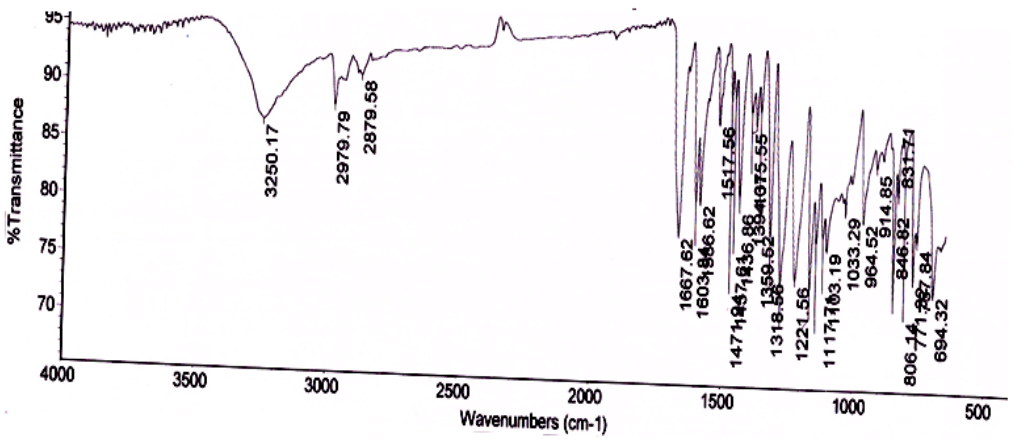


Fig. 5: FTIR spectrum of diclofenac sodium

Calibration curve of diclofenac sodium

Solutions of diclofenac sodium ranging from 2 to 10 µg/ml were prepared in phosphate buffer, pH 7.4. Absorbance was measured for each solution at λmax of 276 nm, using UV-VIS spectrophotometer (Shimadzu, Japan). Correlation coefficient was found to be 0.9973 in phosphate buffer, pH 7.4. The equation obtained is: Y = 0.0023 + 0.0021 X**.** The Standard calibration curve of diclofenac sodium is presented in **Fig. 6**.

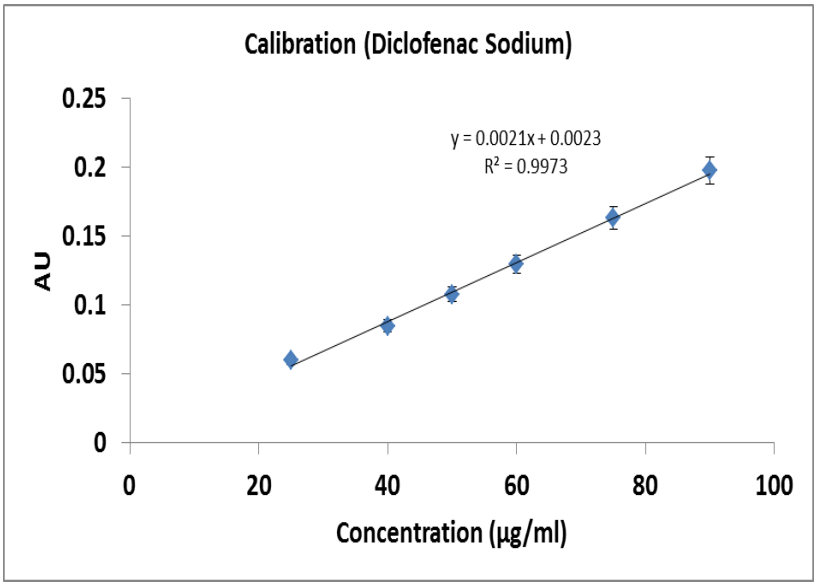


Fig. 6: Standard curve of diclofenac sodium in phosphate buffer, pH 7.4

Preparation and evaluation of drug (diclofenac sodium) loaded films containing extracted gums

Drug loaded films containing extracted *Lepidium sativum gum*

The drug loaded films containing extracted Lepidium sativum gum prepared using glycerin of 0.05 and 0.10 % w/v were found to have dried appearances; whereas, the drug loaded films prepared using glycerin of 0.20 and 0.25 % w/v demonstrated a wet appearance (**Table 10**). However, the drug loaded films containing containing Lepidium sativum gum prepared using 0.15 % w/v glycerin. (LSF3) revealed satisfactory appearances and accepted suitable for further evaluation.

Table 10: Composition of drug loaded films containing extracted Lepidium sativum gum

	LSF1	LSF2	LSF3	LSF4	LSF5
Gum (10 % w/w)	5 ml	5 ml	5 ml	5 ml	5 ml
Glycerine (% w/v)	0.05	0.10	0.15	0.20	0.25
Methyl paraben (% w/v)	0.2	0.2	0.2	0.2	0.2
Diclofenac sodium (% w/w)	0.5	0.5	0.5	0.5	0.5
Appearance	Dried	Dried	Satisfactory *	Wet	Wet

Note: Satisfactory* means films which were suitable for further evaluation

Evaluation of mechanical properties of drug loaded films

The optimized drug loaded film containing extracted Lepidium sativum gum was evaluated for the mechanical properties like weight, mean thickness, folding endurance, water uptake, tensile strength, piercing load, surface pH and drug content uniformity. Weight of the drug loaded film 208.76 ± 0.87 mg/cm2 for LSF4. The mean thicknesses of LSF4 films (drug loaded) were measured as 0.384 ± 0.140 mm. Folding endurance of LSF4 drug loaded films was measured as 251 ± 0.320. The water uptake by LSF4 films loaded with diclofenac sodium was measured 7.38 ± 0.37 %. The tensile strength was calculated as 7.86 ± 0.36 for LSF3

film. The piercing load of LSF4 film loaded with diclofenac sodium was computed as 0.254 ± 0.063 kg. The surface pHs of LSF4 film was measured as 6.70 ± 0.05. The surface pHs of the film was measured and almost neutral pH was observed. The almost neutral pH of the drug free films containing extracted plant gum entails slighter chances of gastrointestinal irritation, when these will be applied as pharmaceutical excipients in the formulations for oral administration. The results of mechanical properties of film containing extracted Lepidium sativum gum are presented in **Table 11**.

Table 11: Mechanical properties of drug loaded films containing extracted gums

Weight (mg/cm^2)	**Mean thickness** (mm)	**Folding endurance** (No. of folds)	**Water uptake** (%)	**Tensile strength** (kg/cm^2)	**Piercing load** (kg)	**Surface pH**	**Content uniformity** (mg/cm^2)
208.76 ± 0.87	0.384 ± 0.140	251 ± 0.320	7.38 ± 0.37	7.86 ± 0.36	0.254 ± 0.063	6.70 ± 0.05	4.90 ± 0.06

Mean ± S.E.; n = 3

Preparation and evaluation of pellets and gum coated pellets containing diclofenac sodium

Preparation of pellets by layering the drug (diclofenac sodium) on non-pareil seeds (nps) of 1.3 mm average size, the drug coated non-pareil seeds (NPS) were prepared.

Scanning electron microscopic (SEM) observation study

The morphology of diclofenac sodium coated pellets Lepidium sativum gum coated pellets were characterized by SEM analyses. The SEM photographs of diclofenac sodium coated pellets are presented in **Fig. 7**. The diclofenac sodium coated pellets were of spherical shaped as seen in the SEM photograph (**Fig. 7A**). The surface topographical morphology of the diclofenac sodium coated pellets showed an almost smooth surface (**Fig. 7B**).

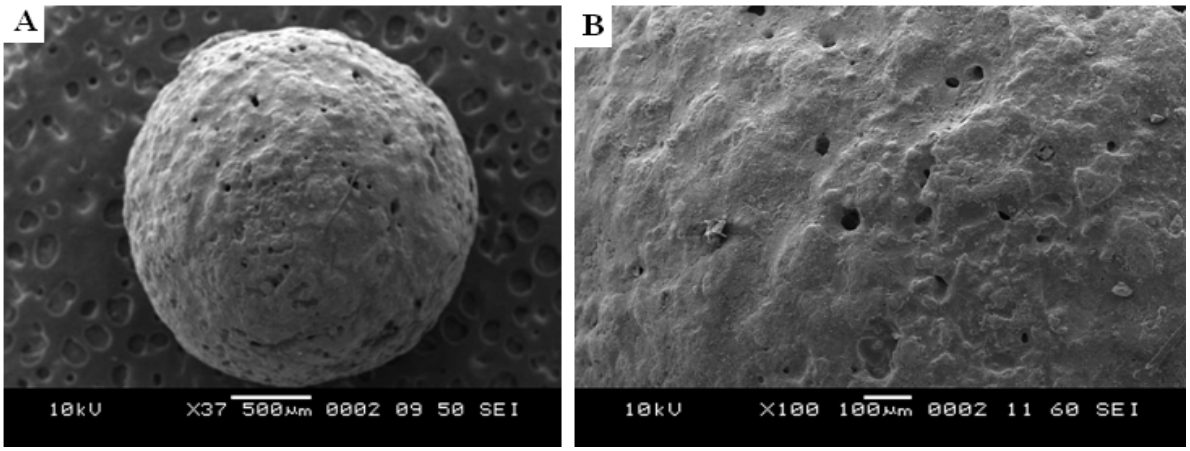


Fig. 7: SEM photographs of diclofenac sodium coated pellets at different magnifications: (A) x 30 and (B) x 100

***In vitro* drug releases from drug (diclofenac sodium) loaded films containing extracted gums**

In vitro drug releases from drug (diclofenac sodium) loaded pallets containing extracted *Lepidium sativum gum* in the phosphate buffer saline, pH 6.8 was evaluated. The diclofenac sodium loaded pallets exhibited sustained drug releasing over a period of 11 hours of dissolution in phosphate buffer saline, pH 6.8. The drug releasing from diclofenac sodium loaded pallets containing extracted Lepidium sativum gum was found sustained. This phenomenon might be due to the higher viscosity of the extracted Lepidium sativum gum.

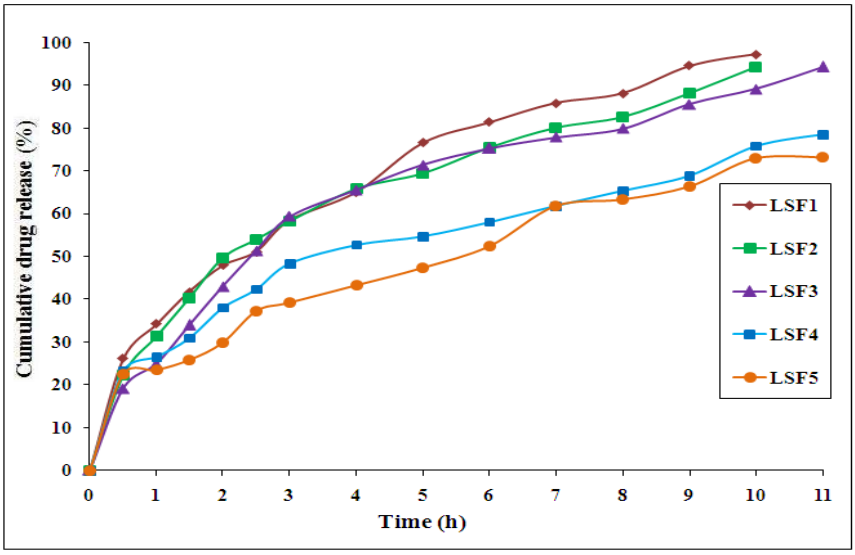


Fig. 8: *In vitro* drug release from diclofenac sodium loaded films containing extracted *Lepidium sativum gum*

In vitro drug releasing data was evaluated kinetically by testing fitting with various mathematical models zero-order model, first-order model, Higuchi model and Korsmeyer-Peppas model. The results of curve-fitting into above mentioned mathematical models are presented in **Table 12** for diclofenac sodium loaded pallets containing extracted Lepidium sativum gum.

When respective correlation coefficients (R^2) were compared, it was found to follow Korsmeyer–Peppas model dominantly with a correlation coefficient closer to 1 for the drug loaded pallets made of the extracted gum. The determined values of release exponent (n) of these prepared films containing diclofenac sodium were calculated as bellow 0.5 which indicate that the drug releasing followed the Fickian (non-steady) diffusion mechanism (when $n \leq 0.5$). Fickian diffusion refers to the solute transport process in which the polymer relaxation time is much greater than the characteristic solvent diffusion time.

Table 12: Curve-fitting results of *in vitro* drug release from diclofenac sodium loaded films containing extracted *Lepidium sativum gum.*

Code	Correlation coefficient (R^2)				Release exponent (n)
	Zero-order model	First-order model	Higuchi model	Korsmeyer-Peppas model	
LSF1	0.9512	0.8612	0.9804	0.9964	0.45
LSF2	0.9266	0.7940	0.9664	0.9862	0.46
LSF3	0.8960	0.7588	0.9673	0.9816	0.49
LSF4	0.9522	0.8649	0.9343	0.9840	0.41
LSF5	0.9701	0.9271	0.9772	0.9861	0.44

Conclusion

In this study an effective film forming capacity of gum extracted from seeds of Lepidium sativum gum on solid dosage form using Diclofenac sodium as a model drug was evaluated. Hence conclude that gum of Lepidium sativum may be potent excipient from natural origin over the existing one.

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