International Journal of Pharmaceutical Sciences and Drug Analysis

E-ISSN: 2788-9254
P-ISSN: 2788-9246
www.pharmacyjournal.info
IJPSDA 2022; 2(2): 22-32
Received: 08-05-2022
Accepted: 12-06-2022

Krishna Kumari J
Department of Pharmaceutics, G. Pulla Reddy College of Pharmacy, Mehdipatnam, Hyderabad, Telangana, India

Bandaru Hemanth Kumar
Department of Pharmaceutics, G. Pulla Reddy College of Pharmacy, Mehdipatnam, Hyderabad, Telangana, India

Prasanthi D
Department of Pharmaceutics, G. Pulla Reddy College of Pharmacy, Mehdipatnam, Hyderabad, Telangana, India

Corresponding Author:
Prasanthi D
Department of Pharmaceutics, G. Pulla Reddy College of Pharmacy, Mehdipatnam, Hyderabad, Telangana, India

Natural gums and mucilage as gelling agents in topical gel formulation

Krishna Kumari J, Bandaru Hemanth kumar and Prasanthi D

Abstract
The study was conducted to evaluate the gelling efficiency of natural gums (tamarind seed gum) and mucilage (Moringa mucilage) using ibuprofen as model drug. Topical drug delivery (TDS) eliminates the first pass metabolism and improves bioavailability and gives good results compared against oral delivery system. Hydrogels are dispersions of network of polymer chains in water as colloidal gels. Ibuprofen is used to relieve pain and anti-inflammation, it was chosen as a model drug in the preparation of hydrogel for site targeted action and to avoid side effects. Physical properties like solubility, swelling index, loss on drying, flow properties were evaluated, chemical characterization of isolated gum and mucilage revealed that polysaccharides are present. Ibuprofen topical gels with natural gum (tamarind seed gum (1-7%), mucilage moringa mucilage (2-8%) were compared with official xanthan gum (1-4%), guar gum (1-3%) as natural gelling agents and HPMC K4M (1-6%), HPMC K100M (1-6%) and sodium alginate (2-6%) as semi synthetic gelling agents. Drug and excipients are compatible with each other by FTIR studies. The prepared gel formulations were evaluated for clarity, homogeneity, spreadability, drug content, in-vitro diffusion, ex-vivo permeation and stability studies. All formulations have shown better physicochemical properties. Based on the maximum percentage of drug release ibuprofen topical gels by natural polymers tamarind seed gum (5%), moringa mucilage (8%), xanthan gum (4%), guar gum (3%) was optimized. And semi synthetic polymers HPMC K4M (4%), HPMC K100M (3%), sodium alginate (6%) was optimized. NF10 formulation with guar gum (3%) is optimized based on the percentage of drug release (27.0±0.14%) for 8 hrs, flux of (427.2±0.09µg/cm^2/hr), cumulative amount of drug permeated Q8 (329±1.53µg/cm^2) and permeability coefficient of (17.08±1.04 ×10^{-3}cm/hr) when compared with tamarind gum (5%), NF1 (23.8±0.13%), (290±1.04µg/cm^2), (376.6±0.04µg/cm^2/hr), (15.04±0.03×10^{-3}cm/hr) and moringa mucilage (8%), NF3 (14.3±0.19%), (175±0.90µg/cm^2), (227.1±0.03µg/cm^2/hr), (9.08±0.02×10^{-3}cm/hr). The drug release pattern was found to follow first order kinetics and Korsemayer papas release mechanism with Fickian diffusion release. Formulations were found to be stable. Tamarind gum and moringa mucilage were efficient as gelling agent in preparation of ibuprofen topical gel but showed retarding effect when compared with official guar gum.

Keywords: Topical drug delivery system, ibuprofen, anti-inflammatory agent and natural gums

Introduction
Polymers derived from plant origin have evoked tremendous interest because of their diverse applications in drug delivery as a disintegrant, gelling agent, emulsifying agent, and suspending agents and as binders [1]. These natural gums and mucilage's are preferred over the synthetic ones because they are biocompatible, cheap, and easily available than the synthetic ones [2]. Also, the natural excipients are preferred over the synthetic and semisynthetic ones because of their lack of toxicity, low cost, soothing action, availability, and non-irritant nature of the excipients [2, 3]. Gums are formed as a natural phenomenon of the plant in which internal plant tissues disintegrate through a process called gummosis. This in turn form cavities, which exudes transformed carbohydrates called gums. Mucilage's are generally normal products of metabolism (physiological products), formed within the cell (intracellular formation) [4]. Gums readily dissolve in water, whereas, mucilage form slimy masses. Both gums and mucilage's are plant hydrocolloids yielding mixture of sugars and uronic acids on hydrolysis [5]. Tamarind xyloglucan is obtained from the endosperm of the seed of the tamarind tree, Tamarindus Indica (family Fabaceae). Tamarind gum is a polysaccharide composed of glucosyl: xylosyl: galactosyl in the ratio of 3: 2: 1. It is used as gelling agent, thickening, suspending, stabilizers, emulsifying agent[4]. Moringa oleifera Gum is obtained from exudes of stem of Moringa oleifera (family: Moringaceae). The gum is a polyuronide constituting Arabinose, galactose and glucuronic acid [5] 10: 7: 2. It is used as a tablet binder, emulsifiers, gelling agents, suspending agents, stabilizers, and thickeners.

Guar gum, also called guaran, is a galactomannan polysaccharide extracted from guar beans that has thickening and stabilizing properties useful in food, feed, and industrial applications [6]. The guar seeds are mechanically dehusked, hydrated, milled and screened according to application [7]. Xanthan gum can be produced from simple sugars using a fermentation process, and derives its name from the species of bacteria used, campestris. This is the same bacterium responsible for causing black rot to form on broccoli, cauliflower, and other leafy vegetables.

Ibuprofen is a non-selective COX inhibitor and hence, it inhibits the activity of both COX-1 and COX-2 [8]. The inhibition of COX-2 activity decreases the synthesis of prostaglandins involved in mediating inflammation, pain, fever, and swelling while the inhibition of COX-1 is thought to cause some of the side effects of ibuprofen including GI ulceration [9]. Ibuprofen, a BCS class II drug, shows poor water solubility and high permeability across the intestinal membrane. NSAIDS are class of the drugs commonly used to treat acute and chronic arthritis. The major drawback of NSAID'S, is risk of gastrointestinal adverse effects such as peptic ulcer disease, particularly when used for chronic conditions such as arthritis [10]. There is great interest to develop non-oral dosage form of ibuprofen to minimize its gastric side effects, while at the same time delivering consistent drug levels at the application site for prolonged periods. Ibuprofen is available in gel dosage form, marketed in the form of Nurofen gels can be used up to four times in 24 hours, or as directed by a doctor. Leave at least four hours between applications. So, NSAIDS can be formulated as topical application. Hence it has been envisaged to formulate ibuprofen topical gel to avoid the systemic side effects, using natural gums, mucilage such as tamarind seed gum and moringa, xanthan, guar gum as gelling agent. And comparison with synthetic gelling agents.

Materials and methods

Materials

Ibuprofen was gifted by Medico Remedies Pvt. Ltd., tamarind seed powder was purchased from Local Market, moringa gum was purchased from Jagadish enterprises, xanthan gum & guar gum was purchased from Yarrow chem products, Carbopol was gifted from RA Chem pharma Ltd., glycerin, propylene glycol, isopropyl alcohol, benzoic acid, tri-ethanolamine were procured from S.D. Fine Chemicals Ltd.

Drug-excipient compatibility study

Interactions by FTIR

The spectrum analysis of pure drug and physical mixture of drug with different excipients which are used for preparation of gel was studied by FTIR. FTIR spectra were recorded by preparing potassium bromide (KBr) disks using a shimadzu (Koyto, Japan) facility (model-8400S). Potassium bromide (KBr) disks were prepared by mixing few mg of sample with potassium bromide by compacting in a hydraulic press under vacuum at 6-8 tons pressure. The resultant disc was mounted in a suitable holder in IR spectrophotometer and the IR spectrum was recorded from 4000cm to 500 cm in a scan time of 12 minutes. The resultant spectrum was compared for any spectra changes. They were observed for the presence of characteristic peaks for the respective function [11].

Isolation of natural polymers

Isolation of tamarind seed gum

To 20 g of tamarind seed powder, 200 ml of cold distilled water was added and slurry was prepared. The slurry was poured into 800 ml of boiling distilled water. The solution was boiled for 20 min under stirring condition in a water bath. The resulting clear solution was kept overnight so that most of the proteins and fibers settled out. The solution was then centrifuged at 5000 rpm for 20 min. The supernatant was separated and poured into twice the volume of absolute ethanol by continuous stirring. The precipitated mass was pressed between felt. The precipitate was washed with absolute ethanol, diethyl ether and then dried at 50-60°C under vacuum. The dried material was ground and sieved through 100 mesh and stored in a desiccator until used for further studies [12].

Fig 1: In the extraction of tamarind seed gum a) Precipitated mass and b) tamarind seed gum powder.

Isolation of Moringa gum

The gum was collected from trees (injured site). It was dried, ground, and passed through sieve no 80. Dried gum (10 g) was stirred in distilled water (250 ml) for 6-8 h at room temperature. The supernatant was obtained by centrifugation. The residue was washed with water and the washings were added to separated supernatant. The procedure was repeated four more times. Finally, the supernatant was made up to 500 ml and treated with twice the volume of acetone by continuous stirring. The precipitated material was washed with distilled water and dried at 50-60° under vacuum and sieved to form mucilage powder [5].

Fig 2: In the extraction of moringa gum a) Precipitated mass and b) moringa mucilage powder.

Evaluation of isolated tamarind seed gum and moringa mucilage

Organoleptic evaluation of isolated gum and mucilage powder

The isolated gum powder and mucilage powder was characterized for organoleptic properties such as color, odor, taste, fracture, and texture.

Solubility of isolated gum and mucilage

One part of dry gum and mucilage powder separately was shaken with different solvents and solubility was determined [13].

pH of gum and mucilage powder

The gum and mucilage powder were weighed and dissolved in water separately to get a 1% w/v solution. The pH of solution was determined using digital pH meter.

Swelling index

The swelling index is the volume (in ml) taken up by the swelling of 500 mg of test material under specified conditions. The swelling index of the gum and mucilage powder was determined by accurately weighing 500 mg of gum and mucilage powder separately which was further introduced into 25 ml glass-stoppered measuring cylinder 25ml of water was added and mixture was shaken thoroughly every 10 min for 1 hr. It was then allowed to stand for 3 hrs at room temperature. Then the volume occupied by gum, was measured. The same procedure was repeated thrice and the mean value was calculated [14].

Loss on drying

Specific amount of fresh mucilage was taken and its weight was measured and it was placed in a hot air oven maintained at temperature 70 °C for 30 minutes. After 30 minutes, the sample was weighed and the process was repeated till constant weight was achieved. Final Loss on drying is calculated using formula

$$\text{LOD (\%)} = \frac{\text{mass of water in sample}}{\text{total weight of wet sample}} x100$$

Micromeritic properties of isolated gum and mucilage powder [15]

Bulk density

The bulk density, ρ_b, is obtained by adding a known mass of powder to a graduated cylinder. The density is calculated as mass/volume. It is determined using the formula

$$\rho_b = \frac{\text{Weight in gms}}{\text{Vb (bulk volume)}}$$

Tapped density

The tapped density, ρ_t, is obtained by mechanically tapping a graduated cylinder containing the sample until little further volume change is observed. The tapping can be performed using different methods. The tapped density is calculated as mass divided by the final volume of the powder. It is determined using the formula

$$\rho_t = \frac{\text{Weight in gms}}{\text{Vt (tapped volume)}}$$

Angle of repose

Angle of repose is the maximum angle possible between the surface of the pile of the powder and the horizontal plane. The frictional forces in the loose powder can be measured by angle of repose. The tangent of the angle of repose is equal to the coefficient of friction (μ) between the particles. Hence, the rougher and more irregular the surface of the particles, the greater will be the angle of repose. The angle of repose of the mucilage powder was determined by the funnel method. Accurately weighed quantities of powder blend were taken in a funnel and the height of the funnel was adjusted in such a way that the tip of the funnel just touched the apex of the powder blend inside. The powder blend was allowed to flow through the funnel freely onto the surface. The diameter of the pile of the powder blend was measured and the angle of repose was calculated using the following equation:

$\text{Tan } \theta = h/r$; $\theta = \tan^{-1} h/r$

Where,
θ = angle of repose,
h = height of the heap (in cm) and
r = radius of the base (in cm).

Preliminary confirmation test for gum and mucilage powder [15]

Molisch's test

100 mg of dried mucilage powder was taken in a test tube. To this dried mucilage powder Molisch's reagent was added and conc.H_2SO_4 was added along the sides of the test tube.

Ruthenium test

A small quantity of dried mucilage powder was taken on a slide with ruthenium red solution and observed under microscope.

Iodine test

100 mg of dried mucilage powder was taken in a test tube and 1 ml of 0.2N Iodine solution was added to it.

Preparation of gels [16]

Different concentrations of isolated tamarind seed gum powder (1% to 7%), moringa gum mucilage powder (2% to 8%), xanthan gum (1% to 4%), guar gum (1% to 3%), HPMCK4M (1% to 6%), HPMCK100M (1% to 6%) and sodium alginate (2% to 6%) were initially tried as gelling agents. Based on optimum gel consistency, concentration of each gelling agent was selected and then formulated as gels with drug 15%w/w (according to IP monograph). Glycerin or propylene glycol or PEG 400 were added as plasticizer and benzoic acid as preservative. The dispersion was allowed to stand at room temperature for 1 hour to obtain viscous mixture. The required quantity of tri-ethanolamine was then added to gel by mixing gently for adjustment of skin pH (Mishra M.U *et al*., 2011) [13], (Panda D *et al*., 2006) [5]. The formulation table of gels with natural polymers is given in table 1 and with semi synthetic polymers is given in table 2.

Table 1: Formulation of ibuprofen topical gels with different concentrations of natural polymers

Ingredients	NF1	NF2	NF3	NF4	NF5	NF6	NF7	NF8	NF9	NF10
Drug (g)	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Tamarind seed gum (%)	5	7	-	-	-	-	-	-	-	-
Moringa gum mucilage (%)	-	-	8	-	-	-	-	-	-	-
Xanthan gum (%)	-	-	-	1	2	3	4	-	-	-
Guar gum (%)	-	-	-	-	-	-	-	1	2	3

Glycerin (%)	10	10	10	-	-	-	-	-	-	-
Propylene glycol (%)	-	-	-	10	10	10	10	10	10	10
Benzoic acid (%)	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Isopropyl alcohol (ml)	3	3	3	3	3	3	3	3	3	3
Triethanolamine (%)	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
Distilled water	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
Total weight of gel (g)	10	10	10	10	10	10	10	10	10	10

Table 2: Formulation of ibuprofen topical gels with different concentrations of semi synthetic polymers

Ingredients	**SF1**	**SF2**	**SF3**	**SF4**	**SF5**	**SF6**	**SF7**	**SF8**
Drug (g)	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
HPMC K4M (%)	4	5	6	-	-	-	-	-
HPMC K100M (%)	-	-	-	3	4	5	6	-
Sodium alginate (%)	-	-	-	-	-	-	-	6
PEG 400 (%)	10	10	10	10	10	10	10	10
Propanol (%)	30	30	30	30	30	30	30	30
Distilled water	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
Total weight of gel (g)	10	10	10	10	10	10	10	10

The topical gels of ibuprofen were evaluated for the following parameters.

Clarity [17]

Clarity of prepared ibuprofen hydrophilic gel was determined by visual inspection under black and white back ground and it was graded as follows: turbid +, clear ++, very clear +++.

Homogeneity [18]

All developed gels are tested for homogeneity by visual inspection after the gels have been set in the container. They are tested for their appearance and presence of any aggregates.

pH Measurement [19]

The pH of formulated gels is determined by using digital pH meter. 1 g of gel is dissolved in 100 ml distilled water and stored for two hours. The measurement of pH of each formulation is done in triplicate and average values are calculated.

Viscosity Measurement [20]

Viscosity is an important parameter for characterizing the gels as it affects the extrudability and release of drug. Viscosity of prepared gels was determined by Brookfield programmable viscometer LVDV-II+PRO. The spindle number 64 was rotated at 20rpm. Samples of the gels were allowed to settle over 30 minutes at the temperature (25±1°C). Rheological behaviour of all formulated gels systems was studied. In gel system, consistency depends on the ratio of solid fraction, which produces the structure to liquid fraction.

Spreadability [21]

For the determination of spreadability, 1g of sample was applied between the two 20x20cm glass slides and was compressed to uniform thickness by placing 100 g weight for 1min. The distance moved by gel due to pressure was measured as length. Spreadability (S) was calculated using the formula.

$$S = M.L / T$$

Where,

S = Spreadability,
M = Weight tide to the upper slide,
L = distance moved by gel,
T = Time of study.

Extrudability [21]

The extrudability test was carried out by Pfizer hardness tester. A 15 gm of gel was filled in aluminum tube. The plunger was adjusted to hold the tube properly. The pressure of 1kg/cm² was applied for 30 sec. The quantity of gel extruded was weighed. The procedure was repeated at three equidistance places of tube. Test was carried in triplicate.

Drug content

An amount of formulated gel equivalent to 5mg ibuprofen was weighed and immersed in a 100 ml volumetric flask containing 80 ml of phosphate buffer saline (pH 7.4). The flask was stoppered and placed in a mechanical shaking water bath set at 37˚C for 2 hrs to allow for complete dissolution of the drug and made up to volume with phosphate buffer saline pH 7.4. A 20 ml aliquot of this solution was withdrawn and placed in 100 ml volumetric flask and the volume made up using phosphate buffer saline (pH 7.4). The UV absorbance of the solution was read at 224nm using phosphate buffer saline pH 7.4 as the blank [22] (Patel H K *et al*., 2018).

***In-Vitro* Drug Release Studies by Diffusion studies** [23]

The formulated gels were studied employing the permeation apparatus as described by (Fites *et al*., 1970). A glass cylinder with both ends open, 10cm height and 3.7 cm outer diameter was used as a permeation cell. Dialysis membrane (cut to suitable size, washed in distilled water and soaked in phosphate buffer saline pH 7.4) was fixed to one end of the cylinder. 500 mg of the prepared gel was taken in the cell (donor compartment) and the cell was immersed in a beaker containing 250 ml of (receptor compartment). The cell was immersed into a depth of 1cm below the surface of buffer, which was agitated by magnetic stirrer and the temperature was maintained at 37˚±1˚C throughout the experiment. Aliquots were withdrawn from the receptor compartment periodically (15mins, 30mins, 1, 2, 3, 4, 5, 6, 7, 8hrs). After each withdrawal, the volume of liquid in the receptor compartment was replaced by phosphate buffer saline pH 7.4. The drug concentration was determined

spectrophotometrically at 224nm.

Comparison between natural and semi synthetic polymers of ibuprofen topical gels

Based on the percentage of drug release the optimized ibuprofen topical gel of natural polymer is compared with the optimized ibuprofen topical gel of semi synthetic polymers**.**

Ex-vivo permeation studies [24]

For the permeation studies locally fabricated Franz diffusion cells with 25 ml receptor volume were used. The thawed rat skin was mounted onto diffusion cell such that the dermis side was in constant contact with receptor solution. 500 mg of gel was applied to the stratum corneum facing the donor compartment and the hydrodynamics in the receptor compartment were maintained by stirring on magnetic stirrer at 600 rpm. 1 ml sample was withdrawn at predetermined time intervals for 24 hours and drug content was analyzed by UV-VIS double beam spectrophotometer at 224 nm.

Ex-vivo permeation rate parameters such as % drug release, cumulative amount permeated in 24hrs (Q_{24}), steady state transdermal flux (SSTF), permeability coefficient and lag time for percutaneous absorption of ibuprofen were calculated.

Steady state flux (µg/cm²/hr)

Steady state flux (J_{ss}) is defined as the rate of diffusion or transport of a substance through a permeable membrane. After reaching the steady state of drug permeation, flux was calculated using the following equation.

$$J_{ss} = \frac{dQ}{A} . dt$$

dQ - amount drug permeated

A - Unit cross-section area

t - Time (t).

The steady state flux obtained by plotting the cumulative amount of drug permeated in micrograms per square centimeter versus time in hours and the slope is the flux.

Permeability coefficient (cm/hr)

The permeability coefficient (Kp) was calculated with the following equation:

$$Kp = \frac{Jss}{CV}$$

Where

cv is the total donor concentration of the formulation

Lag Time (hrs): Lag time is the time required for the drug to get released from the reservoir. It is calculated by plotting cumulative amount of drug permeated vs time. The x-intercept value gives the lag time.

Calculation of model dependent kinetics for prepared gel formulations

Various models were tested for explaining the kinetics of drug release. To analyze the mechanism of the drug release rate kinetics of the dosage form, the obtained data was fitted into zero-order, first order, Higuchi and Korsemeyer-peppas release model, to study the drug release from the dosage form.

Skin irritation studies [25]

Skin irritation studies were performed on rabbits after the approval by the Institutional animal ethical committee. A primary skin irritation test was performed since skin is the vital organ through which the drug is transported. The test was carried out on three healthy rabbits weighing between 1.5-2 kg. Gels was applied (0.5g/animal) twice a day for 7 days. The site was observed for any sensitivity and reaction if any was observed for any sensitivity and reaction if any, was graded 0,1,2,3 for no reaction, slight patchy erythema, slight but confluent or moderate but patchy erythema and serve erythema with or without edema, respectively.

Stability test

Optimised formulations of natural and semisynthetic polymers were subjected to stability at room temperature for one month. The physico chemical properties and drug content were evaluated every week.

Results and discussion

Drug-excipients compatibility studies

Compatibility studies by Fourier Transform Infrared spectroscopy were carried out to study the possible interaction between Ibuprofen and other excipients.

The various FTIR graphs both of pure drug and various excipients in combination are given in Figure no 3, 4, 5, 6, 7 respectively.

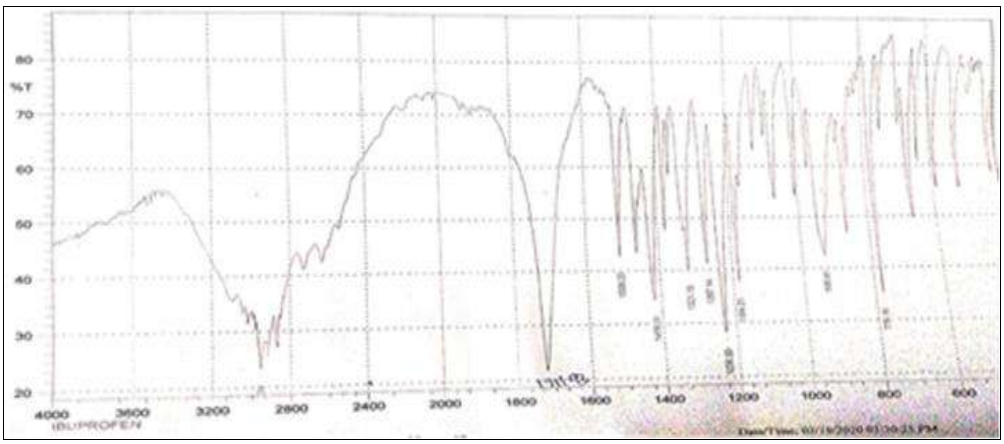


Fig 3: FTIR graph of pure drug (Ibuprofen)

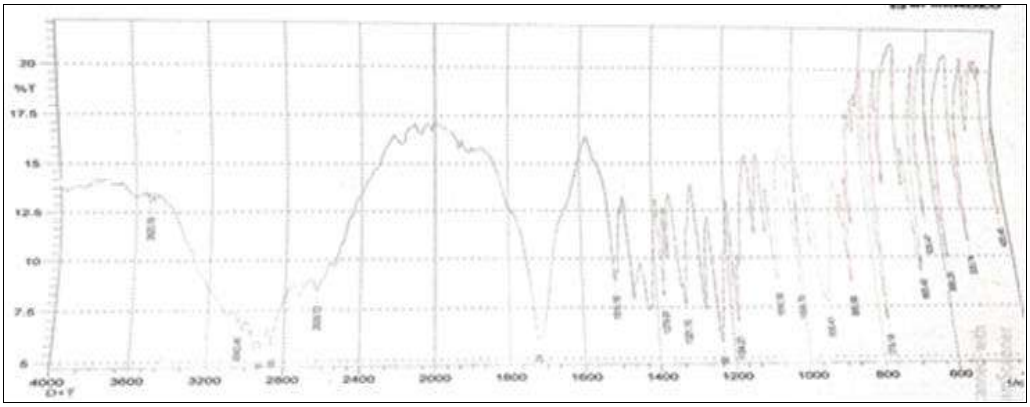


Fig 4: FTIR spectra of Ibuprofen +Tamarind seed gum powder

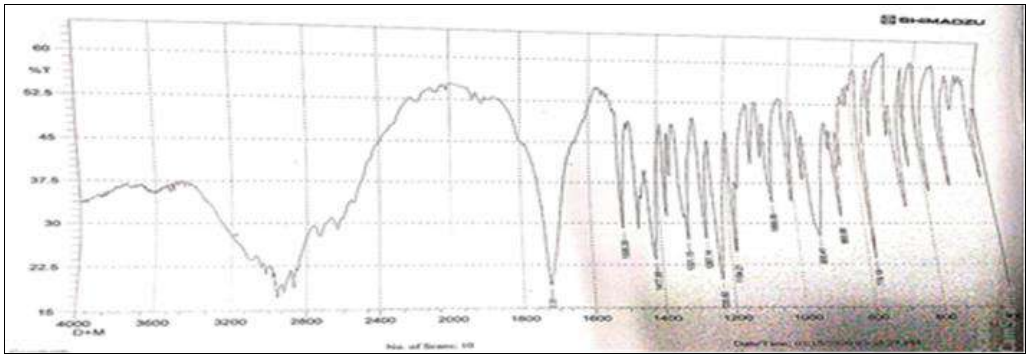
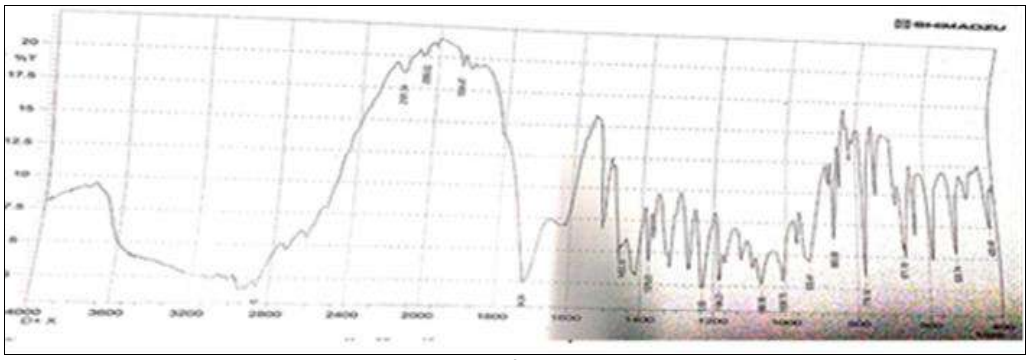


Fig 5: FTIR spectra of Ibuprofen + Moringa gum mucilage



s

Fig 6: FTIR spectra of Ibuprofen + Xanthan gum

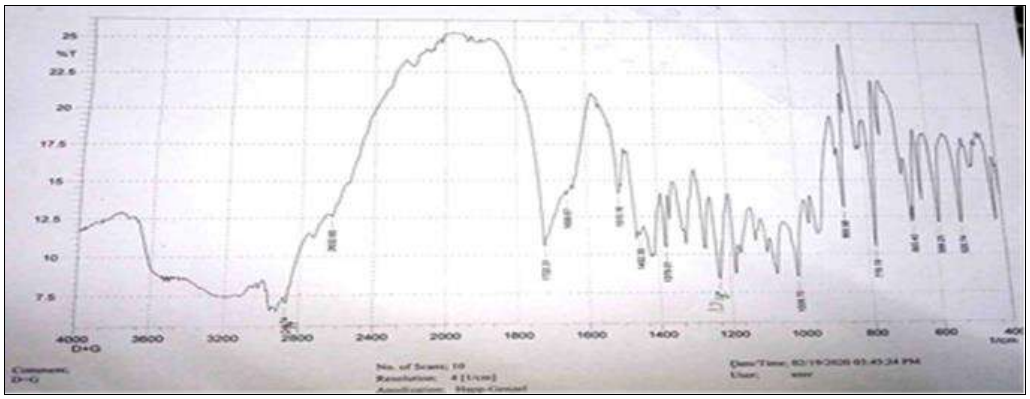


Fig 7: FTIR spectra of Ibuprofen + Guar gum

Table 3: FTIR interpretation of Ibuprofen

S.no.	Region in cm^{-1}	Bond	Functional group
1	1720	C=O stretching	Ketone
2	2953.45	C-H stretching	Aliphatic methylene group
3	2360.44	O-H stretching	Hydroxyl group
4	1227.47	C….C stretching	Alkyl group

The wave numbers of the principal peaks shown in table 3 of Ibuprofen appeared as characteristic peaks in the IR graphs of the pure drug and physical mixture of drug with excipient. This indicates no interaction between drug and excipient and that the pure drug was not altered functionally. Thus, the excipients were found to be compatible. So, polymers can be employed for the topical drug delivery of the ibuprofen.

The isolated gum and mucilage were evaluated for organoleptic, solubility, pH, swelling index, loss on drying and floe properties.

Table 4: Physicochemical properties and flow properties of isolated gum and mucilage

Parameters	Organoleptic	Solubility	pH	Swelling index	Loss on drying (%)	Bulk density g/cc	Tapped density g/cc	Angle of repose (θ)
Tamarind seed gum	Light brownish in color with rough texture and rough fracture, odorless.	Soluble in hot water, insoluble in organic solvent such as benzene, ether, chloroform	6.7	11.2±0.02	0.0052±0.05	0.442±0.04	0.589±0.05	26.5±0.02
Moringa mucilage	White colour but changes to reddish brown or brownish exposure.	Sparingly soluble in water forming viscous solution, insoluble in ethanol methanol, acetone, ether	5.77	19.7±0.94	0.0068±0.06	0.716±0.12	0.895±0.05	30.8±0.01

Note: Values are expressed as Mean ±SD, n=3

The physicochemical properties of isolated gum and mucilage were within limits. Isolated gum and mucilage showed good flow properties. The gum and mucilage showed swelling properties indicating there can be used as gelling agent.

The isolated gum and mucilage powders were evaluated for chemical characterization such as Molisch test, Ruthenium test, and Iodine test. The results given in table 5 confirm the presence of carbohydrates.

Table 5: Chemical characterization of isolated gum and mucilage

S.no	Test	Observation	Inference
1	Molisch test	Violet green colour was observed at the junction of two layers.	Carbohydrate present.
2	Ruthenium test	Pink colour was developed.	Mucilage present
3	Iodine test	No colour was developed in the solution.	Polysaccharides present.

Note: Values are expressed as Mean ±SD, n=3

All the prepared ibuprofen topical gels with natural polymers and synthetic polymers were evaluated for their physicochemical properties such as clarity, pH, viscosity, spreadability, extrudability, homogeneity, and drug content. The results are given in table 6 and table 7. The gels were found to be clear, homogenous [26], with optimum pH for skin application, optimum viscosity required for gel formulation, good spreadability, better extrudability from packaging and drug content.

Table 6: Evaluation of ibuprofen topical gel with natural polymer for physicochemical properties

Formulation code	Clarity	Homogeneity	pH	Viscosity (Cps)	Spreadability (mg.cm/sec)	Extrudability	Drug content%
NF1	+++	++	5.91±0.03	40300±170	11.4±0.3	+++	99.41 ± 0.22
NF2	+++	+++	5.62± 0.13	35600±120	12.2±0.09	+++	99.41 ± 0.28
NF3	+++	+++	5.74±0.03	40300±170	18.3±0.06	++	97.98 ± 0.60
NF4	+++	+++	6.86±0.07	34700±140	14.2±0.09	+++	97.21 ± 0.9
NF5	+++	+++	6.82±0.02	35600±120	20.6±0.06	+++	99.41 ± 0.28
NF6	+++	+++	6.89±0.02	40300±170	21.2±0.05	+++	98.29 ± 0.5
NF7	+++	+++	6.76±0.10	41600±180	20.4±0.08	++	99.21 ± 0.22
NF8	+++	++	6.22± 0.14	34700±140	11.5±0.07	+++	99.45 ± 0.37
NF9	++	++	6.26±0.10	39700±110	12.2±0.06	++	98.01 ± 0.28
NF10	+++	++	6.31±0.50	38300±170	14.6±0.05	+++	99.48 ± 0.60

Note: Values are expressed as Mean ±SD, n=3

Clarity: +++ very clear, ++ clear, + turbid; Homogeneity & Extrudability : +++ Excellent, ++ good, + satisfactory

Table 7: Evaluation of ibuprofen topical gel with semi synthetic polymer for physicochemical properties

Formulation code	Clarity	pH	Homogeneity	Spreadability (mg.cm/sec)	Extrudability	Drug content%	Viscosity (Cps)
SF1	+++	6.2± 0.11	+++	21.4±0.3	+++	98.01 ± 0.28	33600±160
SF2	+++	6.7± 0.13	+++	21.2±0.9	+++	97.98 ± 0.60	38200±130
SF3	+++	6.0±0.03	+++	16.3±0.6	++	99.13 ±0.99	39700±110
SF4	+++	6.6± 0.07	+++	18.2±0.9	+++	97.21 ± 0.9	34300±170
SF5	+++	6.4±0.09	+++	17.6±0.6	+++	99.41 ± 0.28	35600±120
SF6	+++	6.2±0.02	+++	23.2±0.05	+++	98.29 ± 0.5	40300±170
SF7	+++	6.2±0.13	+++	16.4±0.8	++	99.21 ± 0.22	41600±180
SF8	+++	6.7± 0.14	+++	17.5±0.7	+++	95.45 ± 0.37	34700±140

Note: Values are expressed as Mean ±SD, n=3

Clarity: +++ very clear, ++ clear, + turbid; Homogeneity & Extrudability: +++ Excellent, ++ good, + satisfactory

In vitro diffusion study was determined by dialysis membrane and the graphs are given in figure 8, 9, 10, 11. From the results, it was seen that NF1 formulation containing tamarind seed gum 5% showed 23.8±0.13% release for 8 hrs, NF3 formulation containing moringa mucilage 8% showed 14.3±0.19% release for 8 hrs, NF7 formulation containing xanthan gum 4% showed 14.4±0.11% release for 8 hrs, NF10 formulation containing guar gum 3% showed 27.0±0.13% release for 8 hrs. So, these are optimized, and further compared with the optimized ibuprofen topical gels of semi synthetic polymers. In- vitro release studies it was seen that SF1 formulation containing HPMC K4M 4% showed 17.47±0.21% release for 8 hrs, SF4 formulation containing HPMC K100M 3% showed 19.17±0.09% release for 8 hrs, SF8 formulation containing sodium alginate 6% showed 10.2±0.13% release for 8 hrs.

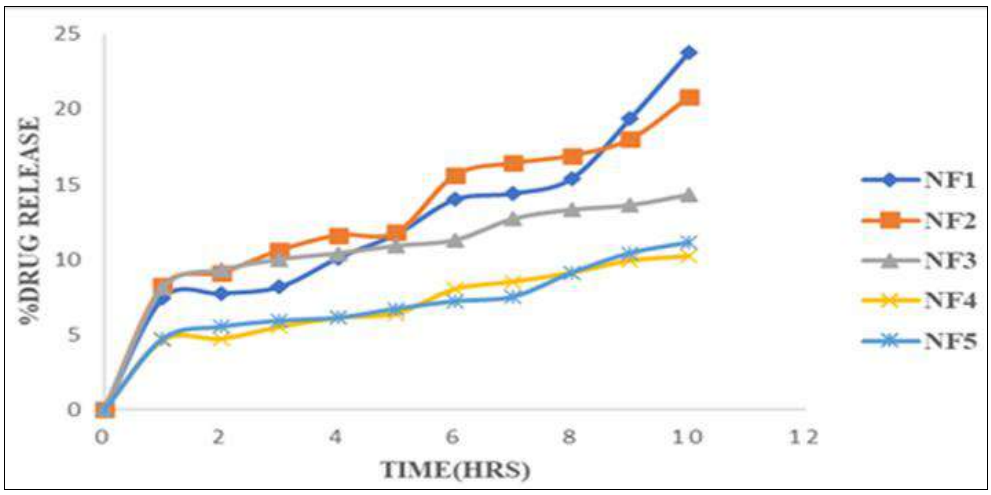


Fig 8: Graphical representation of percentage drug release of topical ibuprofen gel (NF1- NF5) through dialysis membrane

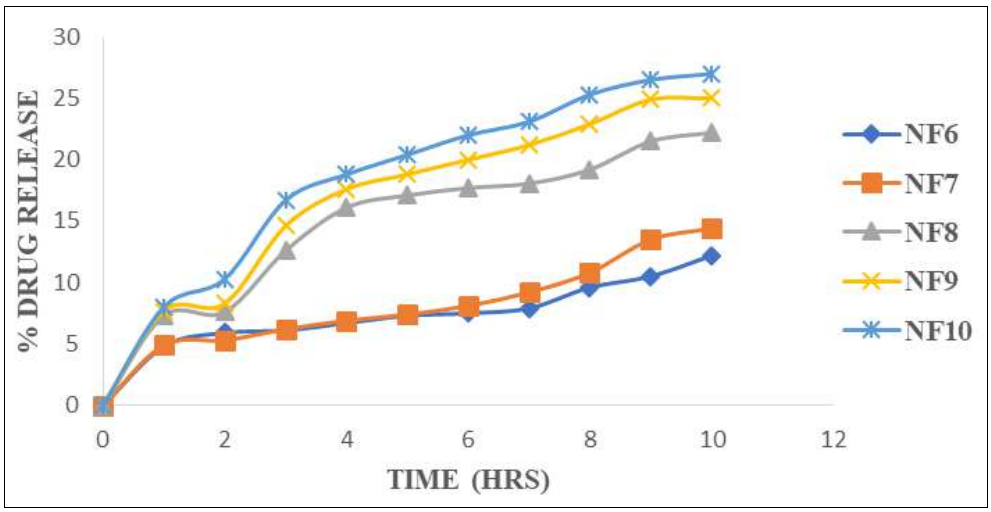


Fig 9: Graphical representation of percentage drug release of topical ibuprofen gel (NF6- NF10) through dialysis membrane

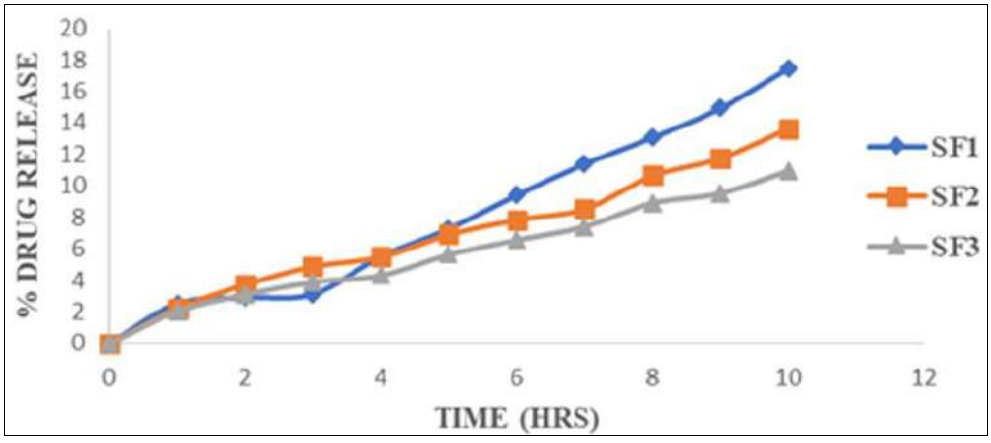


Fig 10: Graphical representation of percentage drug release of topical ibuprofen gel (SF1- SF3) through dialysis membrane

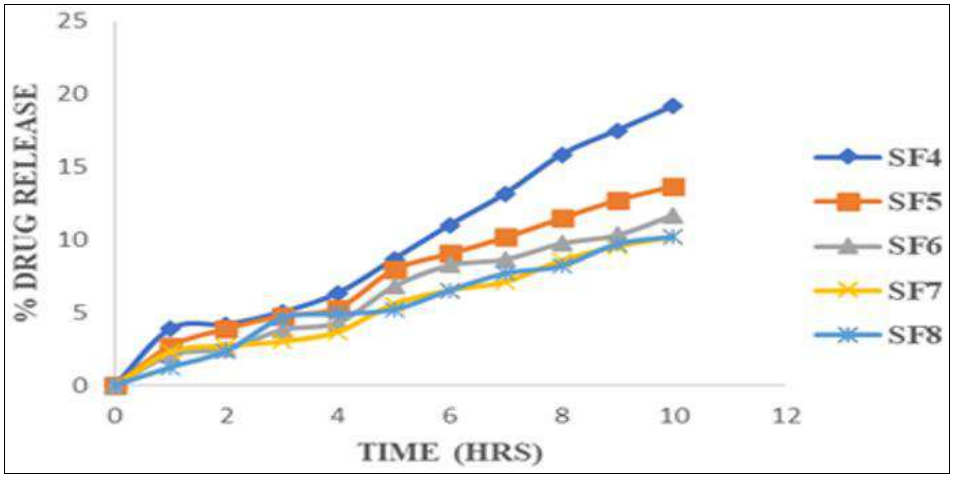


Fig 11: Graphical representation of percentage drug release of topical ibuprofen gel (SF4- SF8) through dialysis membrane

These optimised formulations were further evaluated for ex-vivo permeation studies using rat abdominal skin. The percent drug release graph is given in figure 12 and permeability parameters are given in table 8. From table 8, the formulation NF10 was shown the maximum cumulative amount permeated of drug Q_8 329±1.53 µg/cm², flux 427±0.09µg/cm²/hr permeability coefficient 17.08±1.04cm/hr×10^{-3}.

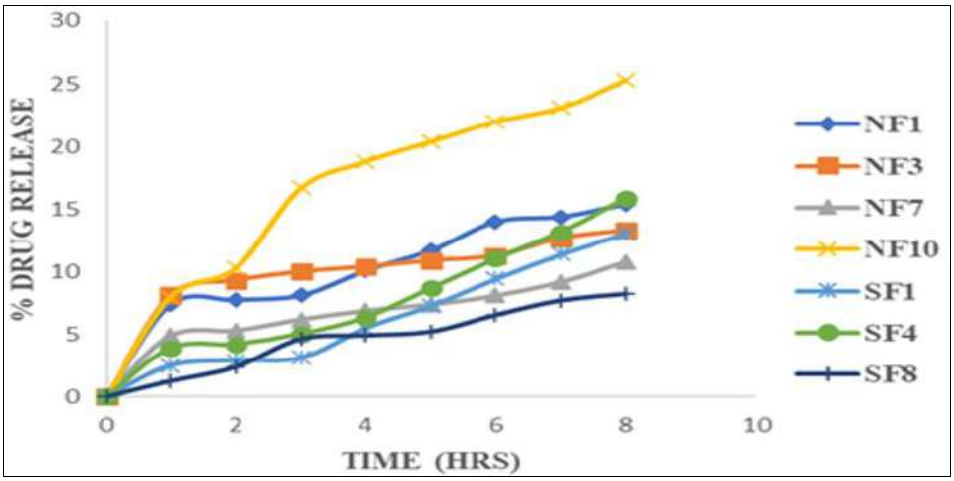


Fig 12: Ex-vivo permeation of ibuprofen topical gel of natural polymers and semi synthetic polymer

Table 8: Permeability parameters of drug /through the dialysis membrane of optimized formulations

Formulation	Q_8 (µg/cm²)	Flux(µg/cm²/hr)	Permeability coefficient (cm/hr×10^{-3})
NF1	290±1.04	376.6±0.04	15.04±0.03
NF3	175±0.90	227.1±0.03	9.08±0.02
NF7	175±2.00	227.2±0.02	9.08±0.04
NF10	329±1.53	427.2±0.09	17.08±1.04
SF1	195.1±0.90	253.2±0.06	10.1±0.02
SF4	226±1.04	293.5±0.04	11.7±0.04
SF8	140±2.38	181.8±0.03	7.24±0.03

Note: Values are expressed as Mean ±SD, n=3

From the drug release kinetics given in table 9 the formulations were found to follow first order kinetics and Korsemayer peppas release mechanism with Fickian diffusion release.

Table 9: Model dependent release kinetics of optimized formulations

Formulations	r^2				n	Release mechanism
	Zero	First	Higuchi	Peppas		
NF1	0.9489	0.9366	0.8763	0.86	0.3112	Fickian diffusion
NF3	0.9615	0.9637	0.9639	0.9336	0.1491	Fickian diffusion
NF7	0.9567	0.9515	0.878	0.8537	0.2901	Fickian diffusion
NF10	0.8641	0.8857	0.9514	0.9652	0.34	Fickian diffusion
SF1	0.9973	0.9958	0.953	0.9423	0.5887	Fickian diffusion
SF4	0.9954	0.9941	0.9473	0.9239	0.4879	Fickian diffusion
SF8	0.9444	0.9491	0.9655	0.9502	0.5378	Fickian diffusion

The formulations were evaluated for skin irritation studies using rabbit model. Formulations did not produce any signs of erythema or edema. Formulations were also found to be stable at room temperature for a period of one month.

Conclusion

Ibuprofen topical gels were prepared for site targeted action and to avoid the side effects using natural polymers such as (tamarind seed gum, moringa mucilage, xanthan gum, guar gum) and semi synthetic polymers such as (HPMC K100, HPMCK4, sodium alginate). Isolated natural gums such as (tamarind seed gum, moringa mucilage) was extracted by using absolute ethanol, acetone as non-solvent. Physicochemical characteristics such as solubility, swelling index, loss on drying, pH, flow properties showed excellent results. Molisch's test, Ruthenium test, Iodine test were studied and revealed presence of polysaccharides. Different concentrations of isolated natural gums tamarind seed gum (1-7%), moringa mucilage (2-8%) natural polymers xanthan gum (1-4%), guar gum (1-3%) were used as natural gelling agents for formulating topical gels, and different concentrations of semi synthetic polymers HPMC K4M (1-6%), HPMC K100M (1-6%) and sodium alginate (2-6%) were used as semi synthetic gelling agents for formulating topical gels. Fourier transform infrared (FTIR) spectrophotometer has been used to study the drug excipient compatibility studies showed that the drug and excipients were compatible with each other. The gel formulation showed good physico chemical properties. From in-vitro comparison studies it is revealed that NF10 formulation containing with 3% guar gum was shown 27.0±0.13% higher percentage of drug release for 8hrs is optimized. From the above results the isolated gum NF1 formulation containing tamarind seed gum (5%) had shown 23.8±0.13% release in 8 hrs. And the mucilage NF3 formulation containing moringa mucilage (8%) has shown 14.3±0.19% release in 8hrs, their gel consistency and clarity were good. This indicates the isolated gum and mucilage can be used as gelling agent. Their percentage release of drug indicates they can be used for topical drug delivery. The permeability parameters for optimized formulation NF10 containing guar gum (3%) has shown flux of 427.2±0.09 µg/cm^2/hr. Cumulative amount of drug permeated/area Q_8 329.2±1.53 µg/cm^2 and Permeability coefficient of 17.08±1.04 cm/hr×10^{-3}. From the drug release kinetics for optimized ibuprofen topical gel formulation NF10 was found to follow first order kinetics and korsemayer peppas release mechanism with fickian diffusion release. The formulations were non-irritant and stable. Hence it is concluded that isolated natural gum and mucilage (tamarind seed gum and moringa mucilage) can be used as gelling agent in formulation of topical gels.

References

1. Kulkarni GT, K Gowthamarajan RR, Dhobe F, Yohanan B. Suresh. Development of controlled release spheroids using natural polysaccharide as release modifier. Drug Delivery. 2005;12(4):201-206. doi: 10.1080/10717540590952537
2. Kokate DCK, Purohit AP, Gokhale SB. Pharmacognosy, Nirali Prakashan, 29th edition, 2008.
3. Jain NK, Misra AN. Controlled and Novel Drug Delivery, CBS Publishers and Distributors, New Delhi,1st edition, 2005.
4. Loveleen Preet Kaur, Rajeev Garg, GD Gupta. Topical gels: A review. Research J Pharm. and Tech 2010;3(1):17-24.
5. Panda D, Swain S, Gupta R, Kanungo SK. Preparation and evaluation of gels from gum of Moringa oleifera. Indian Journal of Pharmaceutical Sciences. 2006;68(6):777-780. Doi:10.4103/0250-474X.31014
6. Nikunj Patel, Ashok Kumar P, Basavaraj, Tom Damien, Someshwara Rao B, Suresh Kulkarni V. Use of Hydrophilic Natural Guar Gum in Formulation of Controlled-Release Matrix Tablets of Metformin Hydrochloride and Its Comparison with Marketed Product. Research J. Pharma. Dosage Forms and Tech 2010;2(2):193-197.
7. Amit Kumar Panigrahi, Mathrusri M, Annapurna Himashankar K. Guar Gum Microspheres of 5-Fluorouracil for Colon Targeting. Research J. Pharm. and Tech 2012;5(2):267-272.
8. Bazigha Abdul Rasool K, Oman Abu-Gharbieh F, Saharan Fahmy A, Heyam Saad S, Saeed Khan A. Development and Evaluation of Ibuprofen Transdermal Gel Formulations. Tropical Journal of Pharmaceutical. 2010;9(4):355-363.
9. Amit Jain K, Rajput Rammulrajsinh, Pradeep Agrawal, Kinal Patel. Design and Evaluation of Sustained Release Matrix Tablets of Ibuprofen. Research J. Pharma. Dosage Forms and Tech. 2011;3(4):142-147.
10. Ghassan Abdullah Z, Muthanna Abdulkarim F. *In vitro* permeation and *in vivo* anti- inflammatory and analgesic properties of nana scaled emulsions containing ibuprofen for topical delivery. International Journal of Nanomedicine 2011;6:387-396. doi: 10.2147/IJN.S14667
11. Mahdi Abd Zair, Prasanthi D, Amoolya Chennuri, Zainab Rahi Hanthal, Lakshmi PK. Effect of Transcutol and Stearylamine on Ibuprofen Hydrophilic Gel for Transdermal Delivery. International Journal of Drug Delivery Technology 2018;8(1):6-14. doi: 10.25258/ijddt.v8i01.11901
12. Kailas Mali K, Shashikant Dhawale C, Remeth Dias J. Extraction, Characterization and Functionalization of Tamarind Gum. Research J Pharm. and Tech 2019;12(4):1745-1752. doi:10.5958/0974-360X.2019.00292.0
13. Mishra MU, Khandare JN. Evaluation of tamarind seed polysaccharide as a biodegradable carrier for colon specific drug delivery. International Journal of Pharmacy and Pharmaceutical Sciences 2011;3(1):139–142.
14. Shruti Panwar, Sangeeta Loonker. Synthesis of Novel Film of Poly Vinyl Alcohol Modified Guar Gum with Tamarind seed Kernel Powder and its Characterization. Asian J Research Chem 2017;10(5):616-620. doi: 10.5958/0974-4150.2017.00103.
15. Niyaz BB. Formulation and evaluation of Gel containing Fluconazole-Antifungal agent. International Journal of Drug Development and Research 2011;3(4):109-128
16. Prasanthi D, Kuruva Jyothirmai, Lakshmi PK. Optimisation Alfuzosin Hydrochloride Organogels for Transdermal Delivery. British Journal of Pharmaceutical Research 2016;11(2):1-16.
17. Mazher Ahmed and Musharraf Ali. Semisolid Dosage Form: Topical Gel Formulation A Review. World JP'

ceutical Rese 2016;5(12):1256-1268.
18. Hemendrasinh Rathod J, Dhruti Mehta P. A Review on Pharmaceutical Gel. International Journal of Pharmaceutical Sciences 2015;1(1):33-47.
19. Kaur LP, Guleri TK. Topical Gel: A Recent Approach for Novel Drug delivery. Asian Journal of Biomedical and Pharmaceutical Sciences 2013;3(17):1-5.
20. Rathore RPS, Nema RK. Formulation and Estimation of Rheological Parameters of Topical Gels of Ketoprofen. Research J. Pharma. Dosage Forms and Tech 2009;1(3):226-228.
21. Chittodiya P, Tomar RS, Ramchandani U, Manocha N, Agrawal. Topical Gel - A Review. Int. J P'ceutical & Biological Archives 2013;4(4):606-613.
22. Amit Jain, Pradeep Agarwal, Akash Kumawat, Rajput Rammularjsinh, Harshit Gautam. Evaluation and Validated UV- Spectroscopic Method for Estimation of Ibuprofen from Marketed Tablets (Brufen400). Research J Pharm. and Tech 2011;4(4):620-623.
23. Patel RR, Patel KR, Patel MR. Formulation and Characterization of Microemulsion based Gel of Antifungal Drug. Pharma Tutor 2014;2(2):79-89.
24. Lakshmi PK, Pawana S, Aparanjitha Rajpur, Prasanthi D. Formulation and evaluation of membrane-controlled transdermal drug delivery of tolterodine tartarate. Asian J Pharm Clin Res 2014;7(2):111-115.
25. Zatz JL, Kushla GP. Gels. In: Lieberman HA, Rieger MM, Banker GS. Pharmaceutical dosage form: Disperse system, New York: Marcel Dekker 2005, 399-421.
26. Roy Chowdhury S, Singh DH, Gupta R, Masih D. A Review on Pharmaceutical Gel. Int J P'ceutical Rese Bio Science 2012;1(5):21-36.