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Original Research Article

The Effect Of Natural Plant Source 'Chia Seeds' As A Gelling Agent In The Formulation Of Aceclofenac Topical Gel For Acute Pain Therapy

Debashish Mohanty[1]*, Souvik Giri[2], Archana Pattanaik[3]

[1]*,[2,3]Assistant Professor, Department of Pharmaceutics, Sri Jayadev College of Pharmaceutical Sciences , Bhubaneswar , Odisha, India [1]Phone no- 6371227917, [1]Email: dsmohanty95@gmail.com

***Corresponding Author:** Debashish Mohanty

*Assistant Professor, Department of Pharmaceutics, Sri Jayadev College of Pharmaceutical Sciences , Bhubaneswar, Odisha, India Phone no- 6371227917, Email id: dsmohanty95@gmail.com

INTRODUCTION:

Topical drug delivery system has a separate place among various conventional drug delivery systems, due to its popularity because providing of different beneficial approaches likeavoiding fast pass mechanism, surpassing gastrointestinal irritation, metabolic degradation associated with oral drug delivery systems. The topical delivery system otherwise known as the dermatological system is one that applied directly to any external body surface byinunctions (by spreading or rubbing), or by spraying or dusting it on, or by instilling it. Topical drug delivery systems used when other drug delivery system does not show desired efficacy. Topical drug delivery system, in most of the cases designed to implement through the skin. The human skin is the defensive shield which protects us from the biological environment surrounds us. Skin which is an easily accessible organ in the human body due to its major and direct linkage with bloodstream through a highly complex network of capillaries, arterioles and arteries connected to it, is an ideal and preferred site of applications of topical drug delivery. The topical drug delivery system is used to exert a local effect for treating skin disorder or as a tool for delivering drug systemically to produce systemic effects by reaching out targeted tissue. Major groups of solid to semisolid preparations are exploring to use as topical drug delivery systems includes ointments, creams, gels, pastes, aerosols, solutions, etc [1, 2, 5].

Gels have used in cosmetics and pharmaceuticals preparations which often provide a faster release of drug entity independent of water solubility of the drug as compared to creams and ointments as topical drug delivery systems. Gels have various advantages like highly biocompatible with a lower risk of inflammation, low chance of adverse reactions, easy applications. Gels for dermatological use have several good and valuable properties like being thixotropic, greaseless, easily spreadable, easily removed, emollient, non-staining, and compatible with several excipients and water-soluble [3, 8].

The scientists are now supporting the finding of natural sources which is extensively usednow a day's in the pharmaceutical sector for its several favourable properties over synthetic ones. Natural origin excipients, therefore, attractive alternative to synthetic products because of biocompatibility, low toxicity, environmental "friendliness" and low price compared to synthetic products. Naturally obtained products as excipients have diverse applications in drug delivery systems such as - binders, disintegrants, gelling agent, emulsifying agent and suspending agents etc [4, 6, 7, 18- 20].

Salvia hispanica L. Is the naturally occurred herbaceous plant cultivated annually insummertime known for its nutritional values, recently investigated for its various pharmacological activities useful to formulate dosage forms. It is commonly known as chia seeds which is a natural source

of unsaturated fatty acids like omega-3 and omega-6 (α- Linolenic acid), fiber (+30 %), proteins of high biological value, and natural antioxidants such as phenolic compounds including chlorogenic and caffeic acids, quercetin, andkaempferol, as well as high dietary fiber content. Chia helps in preventing cardiovascular diseases, inflammatory and nervous system disorders, and diabetes, among others [9-13].

Here we take aceclofenac as the model drug which is chemically [[[2-[(2, 6, dichlorophenyl) amino] phenyl] acetyl] oxy] acetic acid is an orally effective NSAID of the phenylacetic acid group. It poses a remarkable anti-inflammatory, analgesic and antipyretic properties. The continued use of aceclofenac through oral route causes an ulcerogenic effect, flatulence, indigestion (dyspepsia), vertigo, dizziness, dyspnoea, stomatitis, itching (pruritis).

The objectives of the present study are to strive out; to examine the gelling property of the natural source i.e. chia seeds which are used in the formulation of topical gel of aceclofenac [14-17].

METHODOLOGY:

COLLECTION AND PROCESSING OF CHIA SEED:

The chia seed was collected from the local market of Cuttack, Odisha. The collected seeds were dried in a hot air oven at 37±2 ºC for 24 h. The dried seeds were ground by using a grinding machine. The chia powder was passed through Sieve no # 44. The fine chia powder was dried in Hot air oven at 55±2 ºC for 1 h, stored in an air-dried container for further study.

PHYSICAL EVALUATION OF CHIA SEED POWDER [24, 30, 31]:

The chia seed powder was evaluated for physical parameters like seed appearance and colour, odour and taste, moisture absorption, loss on drying, pH, Total ash value, solubility, foreign organic matter, swelling Index, bulk and tapped density, Carr's index, angle of repose and Hausner's ratio.

Physical State:

The state of the powder was evaluated by physical visualisation and holding it with hands.

Colour:

The colour of seeds powder was physically inspected by visualisation method and the colour was identified by personal experience.

Odour:

The odour of the seeds was checked by smelling and identified by personal experience.

Taste:

A particular was identified by personal experience.

Solubility:

The diversely chosen aqueous mediums were used to test the solubility of the powdered seeds extract like distilled water, ethanol and acetone. A definite quantity of seed powder was weighed and it was put in a test tube. The solvent was added drop by drop with continuous stirring and solubility was determined.

pH:

The pH of the seeds was analysed by using digital pH meter by using distilled water. Before the study, the pH meter was calibrated with a standard buffer solution of pH 4 and 9.2. About 1 % w/v

of a solution of Chia seed powder was prepared and the pH of chia dispersion was determined by dipping the electrode for 2 min at room temperature.

Moisture Content:

Accurately weighed (1 g) powdered fine chia extracts were placed in a pre-weighed Petridis. The Petridis containing chia powder was then kept in a digital moisture balance at 60 °C until a constant weight has arrived. The procedure was repeated three times. Finally, moisture content was calculated in the terms of percentage by the help of following formula.

$$\text{Moisture Content (\%)} = [(W_1+W_2-W_3)/ W_2] \times 100 \quad \text{.....(1)}$$

Where W_1 is the weight of Petridis, W_2 is the weight of powdered chia and W_3 is the weight of Petridis + the weight of dried powder.

Loss on drying:

About 5 g of chia powder was accurately weighed and then transferred into a Petridis which was kept under a hot environment created by a hot air oven at 60 °C for 4 h. Loss on drying was calculated in terms of percentage by mass.

Ash Value:

Ash value determines the quality and purity of the drug. Accurately 2 g coarse powder of chia powder was weighed and transferred into a pre-weighed and tarred silica crucible. Then it was undergone incineration by gradually increasing the heat in a muffle furnace up to 450 °C positively not exceeding the limit, for some h. It was kept in a desiccator, the weight of ash with silica crucible was noted. Then the total ash value was calculated in terms of percentage.

Acid-Insoluble Ash:

Total ash was then washed into a 100 ml beaker with the help of 25 ml dilute HCL and the complete content was then heated for 5 min. The content was then filtered with ash-less filter paper. The residue was again washed in hot water and placed with filter paper in silica crucible allowed to incinerate up to 450 °C for 2 h. After that, the weight of cooled acid- insoluble ash which is kept in desiccators with silica crucible was noted and calculated in terms of percentage.

Water-Soluble Ash:

The above-mentioned process was repeated to get the water-soluble ash by incorporating water in the place of dilute HCl.

Bulk Density:

The loosely packed chia fine powder was subjected to the mechanical bulk density apparatus which consists of 2 cylindrical 250 ml glass tube by placing them into it and measuring the volume by the following formula.

$$\rho_b = (w)/ (V_b) \quad \text{.....(2)}$$

Where ρ_b is the Bulk density of powder in g/cc, w is the mass of powder in g and V_b is the bulk volume in cc.

Tapped Density:

The powder blend of chia contained by measuring cylinder was raised and dropped using a suitable mechanical bulk density apparatus with a fixed nominal rate of 100 taps to determine tapped density,

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by the guidance of the following formula.

$$\text{Tapped density} = w / V_t \text{ (tapped volume)} \quad \ldots\ldots (3)$$

True Density:

It was the density of the natural product i.e. chia seeds fine powder blend itself which was calculated by the help of the following equation.

$$\text{True density } (\rho p) = \text{Weight of powder/True volume of the powder} \quad \ldots\ldots (4)$$

Angle of repose:

Angle of repose is the maximum angle possible between the surface of a pile of powder and the horizontal plane which indicates the flow property of the powder. Angle of repose was measured by the funnel method in which the powder blend of fine chia was allowing to empty from the funnel to a horizontal plane by maintaining a minimum gap of 6.34 mm. Angle of repose was measured by calculating the height of the pile and radius of the pile using the formula mentioned below.

$$\theta = \text{Tan}^{-1}(h/r) \quad \ldots\ldots (5)$$

Where, h= height of pile, r = radius of the base of the pile and θ = angle of repose.

Carr's Index:

This property was also known as compressibility. Carr's index (CI) which was a simple and popular method to know the powder flow characteristics of naturally occurred chia calculatedby down noted equation.

$$CI\ (\%) = [(\text{Tapped density} - \text{bulk density})/ \text{Tapped density}] \times 100 \qquad (6)$$

Hausner's Ratio:

It gives an idea about powder blends morphology which was calculated by the following formula.

$$\text{Hausner's ratio} = \text{Tapped density/ Bulk density} \quad \ldots\ldots (7)$$

Swelling Index:

The swelling index is the volume occupied by 1g of the drug, disintegrates including any adhering mucilage and powder after it has been swollen in aqueous liquid for 24 h. About 1 g of chia powder was accurately weighed and transferred into a 25 ml stopper measuring cylinder. The initial volume occupied by the chia powder was noted and the volume was made up to 25 ml with distilled water. The cylinder was stopped with the stopper and then allowed to shaken gently and kept for 24 h under a careful undisturbed condition. The volume was occupied by the chia powder was noted after 24 h. Swelling index (SI) is expressed in percentage and was calculated by the following equation.

$$SI\ (\%) = [(V_t - V_0)/ V_0] \times 100 \quad \ldots\ldots (8)$$

Where V_0 is the initial volume of the powder in a graduated cylinder and V_t denotes the volume occupied by the swollen powder after 24 h.

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ANALYTICAL STUDY OF ACECLOFENAC [27]:

Scanning of pure drug:

The Aceclofenac solution was prepared by using Phosphate buffer of pH 6.8. The solution was scanned by using the UV-Visible spectrophotometer (Shimadzu, Japan) at the wavelength region of 200 to 400 nm. The corresponding wavelength at which maximum absorbance obtained was determined and recorded as λ_{max}.

Preparation of standard curve of Acceclofenac:

About five standard solution strength (2, 4, 6, 8 and 10 µg/ml) of Aceclofenac was prepared by using Phosphate buffer of pH 6.8, whose absorbance was determined by using UV-Visible spectrophotometer at λ_{max} of 275 nm. From the absorbance data, the calibration curve, regression equation, and coefficient were determined by using MS-Excel Window 10.

PRE-FORMULATION STUDIES OF ACECLOFENAC [32-37]:

Prior to Aceclofenac tablet formulation, pre-formulation studies on Aceclofenac drug was carried out on pre-formulation parameters like colour, odour, taste, fine particle size, flow property (by determining bulk and tapped densities, Hausner's ratio, and Carr's Index), solubility, partition coefficient, melting point and dissolution.

Colour:

The colour of procured drug, Aceclofenac was observed visually against bright light and alsoit was checked in UV Fluorescent chamber to determine its fluorescent nature.

Odour:

The odour of drug was observed personally with great care that no drug particle should enterinto the nostril.

Particle Size:

The particle size of Aceclofenac pure drug was determined by using Optical microscope at a magnification of 10X, using eyepiece and stage micrometre. First, the eyepiece and stage micrometre were calibrated and the size of one division of eyepiece micrometre was calculated. Then drug samples were placed over the stage and the number of division covered by each drug particle was measured.

Partition Co-Efficient:

The octanol (10 ml) was taken as an oil phase and water (10 ml) was taken as an aqueous phase. Both the phases were taken in separating funnel, to which 10 mg Aceclofenac drugwas added. The mixture along with drug was shaken for 20 min and the mixture was kept in rest for 24 h. The aqueous phase was carefully separated from the oil phase. The drug contentin the water phase was analysed using UV-Visible spectrophotometer at the maximum wavelength of 275 nm. The partition coefficient (P) was calculated by using the following equation,

$$P = Co/C_W \quad \text{.....(9)}$$

Where P is partition co-efficient, Co and C_W are drug concentration in oil and water phases.

Structural form study:

The structural form of the drug was determined visually with necked eye and also it was checked in the Microscope to check its structural form either amorphous or crystalline.

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Flow properties study:
The flow properties of the drug were determined by determining bulk density, tapped density, Carr's index, Hausner's ratio and angle of repose.

Bulk Density:
The definite mass of drug was weighed using Electronic Digital balance. The volume of weighed powder drug was measured using a measuring cylinder. The measured volume was treated as Bulk volume. The bulk density was calculated using equation no 3.

Tapped density:
The same weighed mass of drug was tapped using digital bulk density apparatus for 1000taps in a cylinder and the changes in volume were measured. This volume was treated as tapped volume. The tapped density was calculated using the formula mentioned in equationno 4.

Carr's Index (Compressibility Index):
Carr's index (CI) of drug powder was calculated to characterize flow properties by using the formula mentioned in equations no 6.The calculated Compressibility Index value of the drug was correlated and interpreted with the standard value given in U.S.P. to characterize flow properties, data as given in Table 1.

Hausner's Ratio:
The Hausner's ratio of drug powder was calculated to characterize flow properties by using the formula mentioned in equation no 8.

The calculated Hausner's ratio value of the drug was correlated and interpreted with the standard value given in U.S.P. to characterize flow properties, data as given in Table 1.

Table 1. Carr's Index, Hausner's Ratio and corresponding flow property as per U.S.P.

Sl. No.	Carr's Index (%)	Hausner's ratio	Flow property
1	≤10	1.00-1.11	Excellent
2	11-15	1.12-1.18	Good
3	16-20	1.19-1.25	Fair
4	21-25	1.26-1.34	Passable
5	26-31	1.35-1.45	Poor
6	32-38	1.46-1.59	Very Poor
7	>38	>1.60	Very very poor

Angle of repose:
The Angle of repose was determined using falling funnel method. The microcapsules were poured through a vertically placed of height (h). Radius (r) of the heap was measured and the angle of repose (Q) was calculated by using the formula as mentioned in equation no 6.

The calculated value of Angle of repose of drug was correlated and interpreted with the standard value given in U.S.P. to characterize flow properties, data as given in Table 2.

Table 2. Angle of Repose and corresponding flow property as per U.S.P.

Sl. No.	Angle of Repose (°)	Flow property
1	25-30	Excellent
2	31-35	Good
3	36-40	Fair
4	41-45	Passable
5	46-55	Poor

6	56-65	Very Poor
7	>65	Very very poor

Hygroscopicity:

The hygroscopicity of drug was determined by using desiccator containing aqueous Potassium Sulphate solution. The pre-weighed drug was kept in desiccators. In the interval of a specific time, the drug was reweighed. The hygroscopicity was calculated by determining the differences in the weight of drug as per the equation given below.

$$\text{Hygroscipicity (\%)} = [(W_f - W_i)/W_i] \times 100 \qquad \text{---------(10)}$$

Where W_i and W_f are the initial and final weight of drug before and after exposing in the desiccator to moisture. The difference in weight and percentage increased weight of drug was determined, which demonstrated the hygroscopic nature of the drug.

Melting point:

The melting point of the pure drug Aceclofenac was determined by the capillary tube method using digital melting point apparatus. Three numbers of capillary tubes are to be taken. Then one end of the tube is closed by applying heat using Bunsen burner. Then the drug is filled into the capillary tube and the thermometer and one tube filled with the drug is placed in the melting point instrument and the instrument is started and the melting point range is determined. And after completion of the work, the apparatus is allowed to cool down after which next capillary tube is placed and again the temperature range is determined. Similarly, the third tube is also determined for the determination of the melting point range. And finally,the average range is calculated.

Fig 1. Melting point test through melting point apparatus.

Solubility:

In the study, 3 numbers of 100 ml beakers were taken. To these 3 beakers, 10 ml of phosphate buffer of pH 6.8 and 7.4 was added. Into which an excessive amount of drug was dissolved to make the system into a supper saturation state. Then the solutions were kept in the refrigerator overnight. Then from the solution system, 1 ml of solution was pipetted out into the Eppendorf microtubes and then tubes were labelled. Along with these 3 tubes, one extra tube was taken, into which distilled water was placed and then the 4 tubes weight were measured and the weights were kept into a similar weight to get the same centrifugation effective. Then centrifugation was carried out at 60 rpm for 10 min by keeping the tubes in opposite direction to each other. Then 1 ml of the sample was withdrawn from the three solution system into 3 test tubes and 2 ml of blank solutions were to

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be added into the test tube. Then the sample was run against blank in UV-Visible spectrophotometer to obtain the absorbance. Then percentage solubility was calculated by using the standard curve equation. The nature of solubility was calculated as per solubility standard data of IP given in Table 3. The same procedure was adopted to determine the solubility of the drug in 0.1N HCl, 0.1N NaOH, ethanol and acetone.

Table 3. Solubility data of solution as per IP [29].

Sl. No.	Solute Concentration (g)	Solvent volume (ml)	Solubility comment
1	1	1<	Very soluble
2	1	1-10	Freely soluble
3	1	10-30	Soluble
4	1	30-100	Sparingly soluble
5	1	100-1000	Slightly soluble
6	1	1000-10,000	Very very poor soluble
7	1	> 10,000	Insoluble

Dissolution study:

It was carried out in USP XXXI paddle-type 1 dissolution test apparatus using 900 ml of Phosphate buffer of pH 6.8 as dissolution medium. Bath temperature was maintained at (37±1) °C throughout the study. About 100 mg of pure drug Aceclofenac was put in the medium. Paddle speed was adjusted to 50 rpm. An interval of 15 min, five ml of sample was withdrawn with the replacement of 5 ml fresh medium. The collected sample solutions were filtered using Whatman Filter paper no 24. Then the sample solutions were analysed for Aceclofenac content by using UV-Visible spectrophotometer at $\lambda_{max}$of 275 nm.

DRUG – EXCIPIENTS INTERACTION STUDY BY FTIR [21]:

FT-IR studies were carried out to point out drug excipients compatibility issues to prevent degradation of formulations from interactions. The FT-IR spectroscopy of drug sample,powder form of chia seeds and the mixture of both drug and chia powder was carried out by the help of FT-IR instrument (Manufacturer-Bruker, Model-α, Number of scans-36, Resolutions-4, Germany). The samples were examined by the ATR technology (Attenuated Total Reflectance) in transmission mode and scanned over the frequency range of 4000-400 cm^{-1}, which is a non-destructive method and easy to handle.

PRIMARY ASSESSMENT STUDY [26]:

The gel preparation by Chia seed was evaluated by adding different quantities of chia seed (0.2, 0.5, 0.8 and 1 g) in four different beakers. To the all beaker water was added slowlywith constant stirring, till gel was formed.

SECONDARY ASSESSMENT STUDY:

The various gels were prepared by using chia seed, HPMC and HPC at a different concentration as per the formulation given in Table 4. A definite quantity of gelling agentwas taken in a clean beaker, to which distilled water was added. The mixture was kept in rest for one day (24 h). After one day, the mixture was stirred constantly till a gel was formed.The gel was de-aired by keeping the gel over vortexer.

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Table 4. The formulation design of gels using different gelling agents.

Sl. No.	Formulations	Gelling agent	Concentration (%)
1	G1	Chia seed	2
2	G2	Chia seed	4
3	G3	Chia seed	5
4	G4	Chia seed	10
5	G5	Chia seed	15
6	G6	Chia seed	20
7	G7	Chia seed	25
8	G8	HPMC	2
9	G9	HPMC	3
10	G10	HPMC	5
11	G11	HPMC	10
12	G12	HPMC	15
13	G13	HPC	5
14	G14	HPC	10
15	G15	HPC	15

Characterization of Gels:

The various prepared gels were evaluated for colour, odour, consistency, clarity and spread ability.

PREPARATION OF GEL IN COMBINATION OF GELLING AGENTS:

Various gels were prepared as per the formulation given in Table 5 by using a combination ofgelling agents that are chia seed with HPMC in different proportion.

Table 5. Formulation design of gel using a gelling agent in a combination form.

Formulations	Chia seed (mg)	HPMC (mg)	Total weight (g)
CH1	100	100	10
CH2	200	200	10
CH3	300	100	10
CH4	400	200	10

FORMULATION DESIGN AND PREPARATION OF ACECLOFENAC GELS:

Gels were prepared by using Aceclofenac as an active therapeutic drug. The gelling agents used were chia seed alone and in a combination of chia seed with HPMC (Table 6). About 10 g of the gel was prepared for each formulation. A definite quantity of gelling agent was taken in a clean beaker, to which distilled water was added. The mixture was kept in rest for one day (24 h). After one day, the mixture was stirred constantly till a gel was formed. The gel was de-aired by keeping the gel over vortexer.

Table 6. Formulation design of Aceclofenac gels.

Formulations	Gelling agents	Gelling agents (g)	Drug (mg)	DW	Total weight (g)
F1	Chia seed	0.5	100	q.s.	10
F2	Chia seed	1	100	q.s.	10
F3	Chia seed	1.5	100	q.s.	10
F4	HPMC	0.2	100	q.s.	10
F5	HPMC	0.3	100	q.s.	10
F6	HPMC+Chia	0.2+0.2	100	q.s.	10
F7	HPMC+Chia	0.3+0.1	100	q.s.	10

DW – Distilled water, q.s. – Quantity sufficient.

Evaluation of Aceclofenac Gel [22-26, 28]:

The prepared gels were evaluated for colour, odour, consistency and spread ability.

Visual examination:

All developed gel formulae were inspected for their homogeneity; colour, odour, syneresis and presence of lumps by visual inspection after the gels have been set in the container.

pH:

About 1.0 g gel was accurately weighed and dispersed in 100 ml purified water. The pH ofthe dispersion was measured using digital pH meter, which was calibrated before use with a standard buffer solution at 4.0, 7.0and 9.0. The measurements of pH were done in triplicate and average values were calculated.

Spread ability test:

A sample of 0.5 g was pressed between two slides (divided into squares of 5 mm sides) and left for about 5 min where no more spreading was expected. Diameters of spreaded circles were measured in cm and were taken as comparative values for spread ability. The results obtained are the average of three determinations

Consistency:

The measurement of the consistency of the prepared gels was done by dropping a cone attached to a holding rod from afix distance of 10cm in such way that it should fall on the centre of the glass cup filled with the gel. The penetration by the cone was measured from the surface of the gel to the tip of the cone inside the gel. The distance travelled by cone was noted down after 10 s.

Drug content:

A specific quantity (100 mg) of the developed gel was taken and dissolved in 100ml of phosphate buffer of pH 6.8. The volumetric flask containing gel solution was shaken for 2 h on a mechanical shaker to get complete solubility of the drug. This solution was filtered in triplicate by using a Whatmann filter paper no 4, and the drug content was estimated spectrophotometrically at maximum wave length of 275 nm.

In-vitrodrug diffusion study:

Cellophane membrane was used for this study. In Kiescary Chien (KC) diffusion cell, about 1.0 g of the gel was kept in the donor compartment. The entire surface of the membrane was in contact with the receptor compartment containing 30 ml of phosphate buffer solution having a pH of 6.8. The receptor compartment was continuously stirred (250 rpm) using a magnetic stirrer. The temperature maintained was 37 ± 1°C. The study was carried out for 1 hwith the interval of 5, 15, 30, 45 and 60 min. The sample was withdrawn (5 ml) at a predetermined period and the same volume (5 ml) was replaced with fresh phosphate buffer solution. The absorbance of the withdrawn sample was measured at maximum wave length of275 nm to estimate drug aceclofenac.

RESULTS AND DISCUSSIONS:

Physical Evaluation of Chia Seed Powder:

The physical evaluation data of Chia powder is given in Table 7. The Chia powder was soluble in water. The pH of Chia powder was very slightly acidic. The Chia powder moisture absorption capability was very high. Very least foreign organic matter was present in the powder. The flowability of Chia powder was excellent.

Table 7. Physical evaluation data of chia seed.

Parameters	Values	Parameters	Values
Colour	Brownish white	Foreign matter (%)	0.1 <
Odour and Taste	Characteristics and mucilaginous	Swelling Index (%)	19
Solubility	H_2O	Bulk density (g/cc)	0.7142
pH	5.76	Tapped density (g/cc)	0.72
Loss on Drying (%)	7.54	Angle of repose (º)	36.6
Total ash (%)	5.85	Carr's Index (%)	0.8
Moisture absorption (%)	98.7	Hausner ratio	1.00812

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Analytical study of Aceclofenac:

From the scanning report (Fig 2), it was evident that the λ_{max} of Aceclofenac in Phosphate buffer of pH 6.8 was found to be 275 nm. The standard curve data is given in Table 8 and Fig 8. The regression equation was found to be Y = 0.024X - 0.016 and the regression coefficient was found to be 0.996.

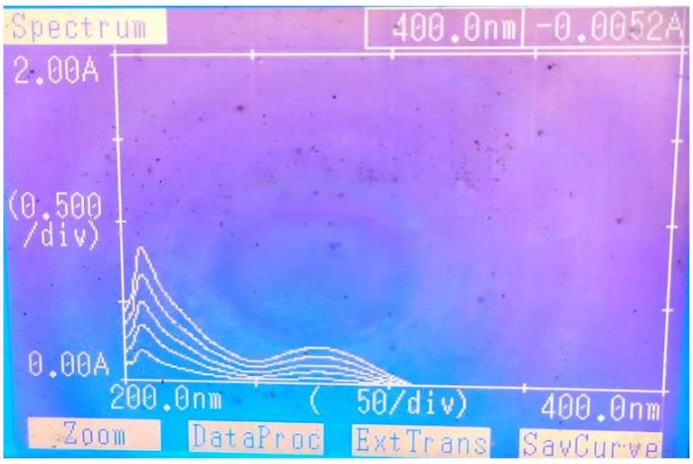

Fig 2. Scanning report of Aceclofenac pure drug in Phosphate buffer of pH 6.8.

Table 8. Standard curve data of Aceclofenac pure drug in Phosphate buffer of pH 6.8.

Sl. No.	Concentration (µg/ml)	Absorbance
1	2	0.0365
2	4	0.0802
3	6	0.1249
4	8	0.1775
5	10	0.2335

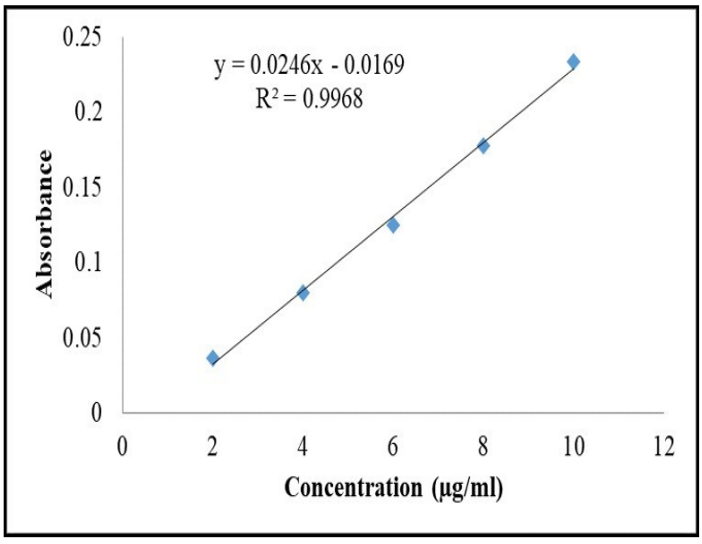

Fig 3. Standard curve of Aceclofenac pure drug in Phosphate buffer of pH 6.8. Table 9. Pre-formulation data of Aceclofenac.

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Table 9. Pre-formulation data of Aceclofenac.

Parameters	Values	Parameters	Values
Colour	White	Melting point	155 ºC
Odour	Less	Partition coefficient	1.26
Taste	Bitter	Bulk density	1.22 g/cc
Nature	Crystalline	Tapped density	1.51 g/cc
Particle size	7.2 µm	Angle of repose	29.7 °
Solubility	Acetone, ethanol	Carr's Index	19.2 %
pH	6.78	Hausner ratio	1.23
Moisture content	5.1 %	Flow nature	Good
Moisture absorption	6.7 %	Dissolution (%) - 1 h	86.2

Pre-formulation studies of Aceclofenac:

The pre-formulation data of pure API drug Aceclofenac is given in Table 9. The Aceclofenac was crystalline in nature. The particle size of Aceclofenac was very less. The aqueous solution of Aceclofenac was very slightly acidic. The moisture content and absorption capacities were very less. The partition coefficient values show that the Aceclofenac was lipophilic in nature. The flowability of Aceclofenac drug powder was good. The amount of drug release in 1 h was comparative good that is 86.2 %.

Drug – Excipients interaction study by FTIR:

No such significant interaction was being found among Aceclofenac and Chia seed as no additional peak being formed or deleted from the IR spectra of Aceclofenac chia seed physical mixture as compared with IR spectra peaks of pure Aceclofenac drug, as evident from the Fig 4.

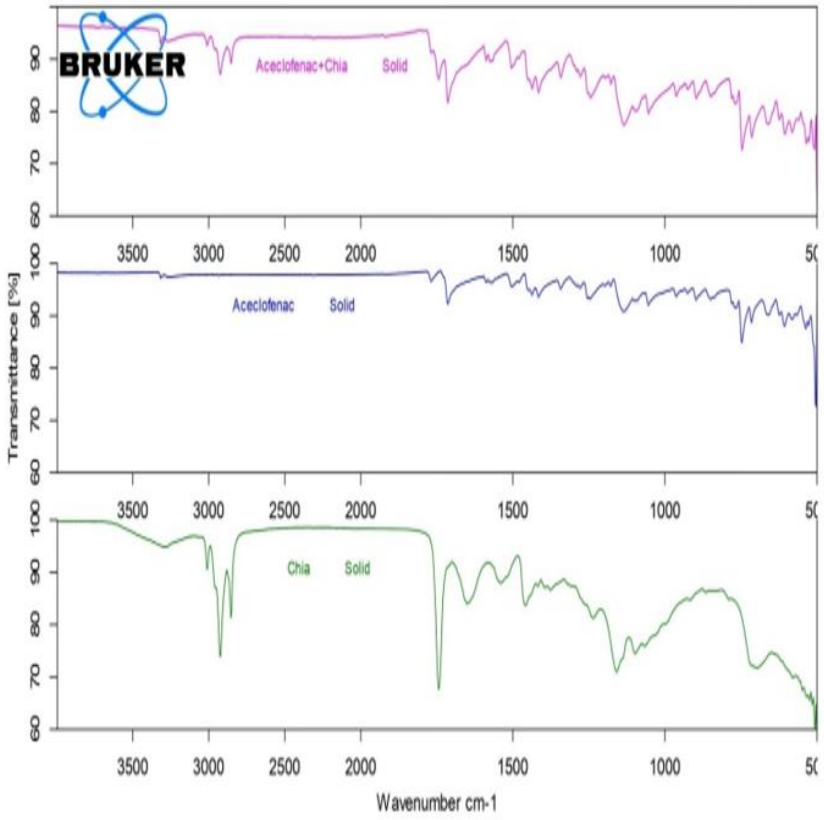

Fig 4. FTIR Spectral data of Aceclofenac, Chia seed and drug chia seed physical mixture in solid-state form.

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PRIMARY ASSESSMENT STUDY:
It was observed that a good consistency gel was formed with chia seed at concentration of 0.5 g of chia seed powder.

SECONDARY ASSESSMENT STUDY:
The results data of gels are presented in Table 10. The consistency of gel formulations G5, G6, G8, G9, G13 and G14 was good. Almost all the gel formulation was odorless. The spread ability was excellent for the gel formulation G8 and G13. The spread ability was good for Gel formulation G5, G6, G9 and G14.

Table 10. The evaluation data of various gels.

Formulations	Colour	Odour	Consistency	Clarity	Spread ability
G1	SB	Slightly	Liquid	Slightly clear	-
G2	SB	Slightly	Liquid	Slightly clear	-
G3	SB	Slightly	Gel with liquid structure	Not clear	+
G4	SB	Slightly	Gel with comparatively low consistency	Not clear	+
G5	SB	Slightly	Good Gel	Not clear	++
G6	SB	Slightly	Comparative good consistency	Not clear	++
G7	SB	Slightly	Hard gel	Not clear	-
G8	CL	OL	Good gel	Clear	+++
G9	CL	OL	Good gel	Clear	++
G10	CL	OL	Comparatively very low hard gel	Clear	+
G11	CL	OL	Hard gel	Not clear	+
G12	CL	OL	Too hard gel	Not clear	-
G13	CL	OL	Good gel	Clear	+++
G14	CL	OL	Good gel	Clear	++
G15	CL	OL	Hard gel	Not clear	+

SDB – Slightly brownish, CL, Colorless, OL – Odorless, - (Poor), + (Fair), ++ Good and +++ (Excellent).

GEL IN COMBINATION OF GELLING AGENTS:
The evaluation data of prepared gel is given in Table 11. The gel formulations CH2 and CH3 were found to be good in consistency. The spread ability was excellent for the gel formulation CH2. The spread ability was good for Gel formulation CH3. The gels were odorless. The good consistency gel possesses very light cream color.

Table 11. Evaluation data gel using the gelling agent in a combination form.

Formulations	Colour	Odour	Consistency	Spread ability
CH1	Colourless	OL	Fair	+
CH2	Very light cream	OL	Good	+++
CH3	Very light cream	OL	Good	++
CH4	Light cream	OL	Fair	+

Colourless, OL – Odourless, + (Fair), ++ Good and +++ (Excellent).ACECLOFENAC GELS USING CHIA SEED:
The evaluation data of Aceclofenac gel by using chia seeed as gelling agent is given in Table 12. The color of gels was either very slight brownish or slightly dark mily color. Some few gels were colorless. All the gel formulations were odorless. The consistency of gel formulation F5 was excellent, whereas the gel formulations F3, F5 and F6 possess good consistency. The pH of gels was in the ranges of 5.5 to 6.1, which was within the skin pH range, thus gel might not be irritating to the skin. Almost all gel formulation possesses very good drug content, that was in the ranges of 83 (F6) to 90 (F7) %.

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Table 12. Various evaluation data of Aceclofenac gels.

Formulations	Colour	Odour	Consistency	pH (X±SD)	Drug content (%) (X±SD)	Spread-ability	CPDR (X±SD)
F1	VSB	OL	-	5.8±0.21	88±0.38	-	21.81±0.98
F2	VSB	OL	+	6.1±0.18	86±0.41	+	10.13±0.84
F3	VSB	OL	++	5.7±0.19	89±0.46	++	4.71±1.02
F4	CL	OL	+	5.9±0.12	86±0.39	+	25.51±0.84
F5	CL	OL	+++	6.0±0.26	85±0.29	+++	12.26±1.05
F6	SDMC	OL	++	5.5±0.22	83±0.44	++	10.46±0.81
F7	SDMC	OL	++	5.7±0.15	90±0.18	++	8.15±0.79

VSB = Very slightly brownish, CL – Colourless, CPDR – Cumulative % drug release, SDMC – Slightly dark milky colour, - (Poor), + (Fair), ++ Good and +++ (Excellent). Drug diffusion for 1 h study. All values are expressed as mean ± standard deviation (n=3). Standard Error of Mean
< 0.606.

The spread ability was excellent for the gel formulation F5. The spread ability was good for Gel formulations F3, F6 and F7. The drug diffusion pattern almost all gel formulations was controlled. Least amount of drug was diffused from gel Formulation F3 containing chia seed 15 %. The drug diffusion manner was constant in gel formulation F2 and F4.

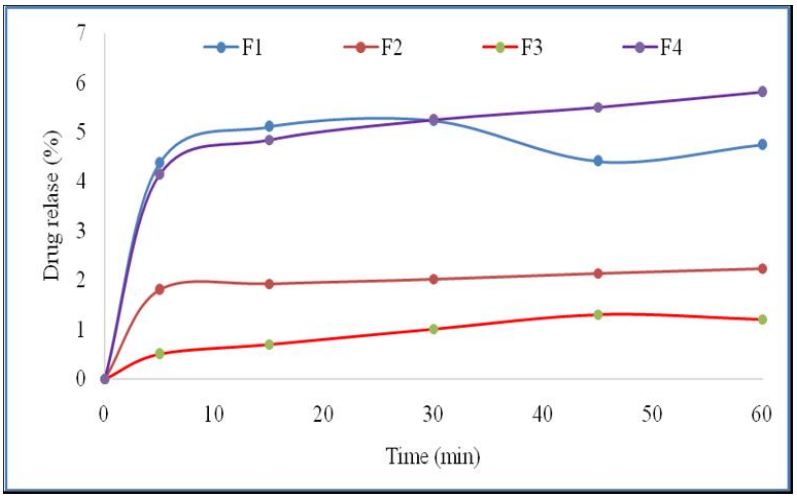

Fig 5. *In vitro* drug diffusion profile of Aceclofenac gel formulations (F1-F4).

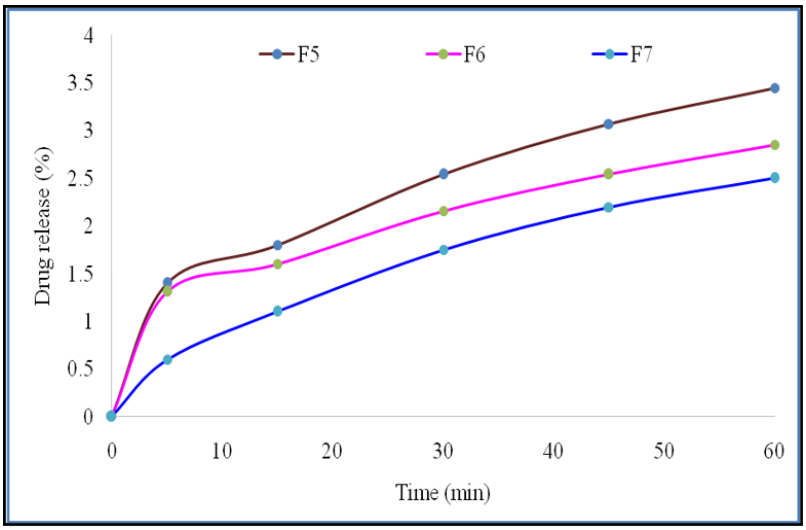

Fig 6. *In vitro* drug diffusion profile of Aceclofenac gel formulations (F5-F7).

CONCLUSION:

The aim of the study was to formulate and evaluate the Aceclofenac topical gel using chiaseed as a gelling agent.

The objectives of the present study were Literature study on chia plant, collection andprocessing of chia seed, physical evaluation of chia powder, the pre-formulation study of Aceclofenac drug, Drug chia seed interaction study by FTIR, primary and secondaryassessment studies for chia seed as a gelling agent, final formulation design, preparation and characterization of Aceclofenac topical gel using chia seed as a gelling agent, selection of optimized formulation and its comparative study with marketed aceclofenac gel formulation. The primarily the gel using chia seed was non toxic to the skin as the pH ranges of preparedgel was within the skin pH range.

Further no such significant drug and chia seed interaction was found from the FTIR study. More over it was found that the gel using chia seed along with HPMC exhibited good gel properties as well as excellent drug release characteristics incomparison to pure chia seed gel. From the above experimental study it significantly evident that the chia seed possesses gelling agent property. The chia seed could be successfully used for the preparation of topical agent. Moreover, the chia seed releasing the drug in a more controlled and constant manner, which could help reduce the side effects of various drugs.

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