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DESIGN AND EVALUATION OF MUCO ADHESIVE SUSTAINED RELEASE TABLETS OF ETODOLAC BY USING NATURAL POLYMERS

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ABSTRACT

The word mucoadhesion is used when the biological substrate is a mucosal surface. With the help of mucoadhesive polymer, we target various absorptive mucosal layers of the body parts which include the ear, nose, eye, gastrointestinal tract, urogenital tract which will get attached on to the related tissue. This system of drug delivery is called as mucoadhesive drug delivery system. The mucoadhesive systems as drug a carrier has been used for maintenance of the residence time at the absorption site, performance its intensified contact with the epithelial barrier. The development of controlled drug delivery system using bioadhesive molecules includes a decrease in dose frequency and an increase in patient compliance. The present study was to formulating the mucoadhesive oral sustained release tablets containing Etodolac as an active ingredient which is used in the treatment of for the short- and long-term relief of rheumatoid arthritis and osteoarthritis. It works by relieving pain and by reducing swelling and inflammation. The present study involves Prolong release of the drug and increased bioavailability leads to significant reduction in the dose and consequently dose related side effects also reduced. In the present research work to formulate mucoadhesive oral Etodolac tablets in order to avoid extensive first pass metabolism and for prolonged effect. Mucoadhesive tablets of Etodolac were prepared by direct compression method using various bioadhesive polymers like Guar gum, gumkaraya and HPMC K15M in different concentration. The present study concludes that mucoadhesive delivery of Etodolac tablets can be a good way to presence of drug at the site of absorption and to prolong duration of

action of drug by reducing the frequency of dosing of Etodolac. The optimised formulation was found to be F6 formulation and its followed peppas release kinetics.

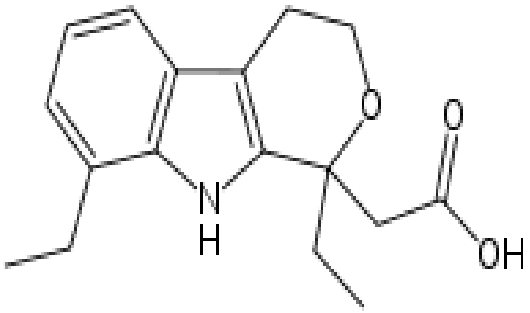
KEYWORDS: mucoadhesion, bioadhesive, Guar gum, gumkaraya.

INTRODUCTION

Etodolac is a non-steroidal anti-inflammatory drug (NSAID) with anti-inflammatory, analgesic and antipyretic properties. Its therapeutic effects are due to its ability to inhibit prostaglandin synthesis. It is indicated for relief of signs andsymptoms of rheumatoid arthritis and osteoarthritis. Chemically it is a(RS)-2-(1,8-Diethyl1-4,9-dihydro-3H-pyrao[3,4-b]indol-1-acetic acid.

Molecular Formula is $C_{17}H_{21}NO_3$ and Molecular Weight is 287.35g/mol and a it is a white crystalline compound. Insoluble in water but soluble in Alcohols, chloroform, Dimethyl sulfoxide and aqueous polyethylene Glycol.

Anti-inflammatory agent, non-steroidal. Cyclooxygenase inhibitor. Mechanism of Action of Etodolac result from inhibition of the enzyme cyclo oxygenase (COX). This decreases the synthesis of peripheral prostaglandins involved in mediating inflammation. Etodolac binds to the upper portion of the COX enzyme active site and prevents its substrate, Arachidonic acid, from entering the active site. Etodolac was previously thought to be a non-selective COX inhibitor, but it is now known to be 5 – 50 times more selective for COX-2 than COX-1. Antipyresis may occur by central action on the hypothalamus, resulting in peripheral dilation, increased cutaneous blood flow and subsequent heat loss.



Structure of Etodolac.

EXCIPIENT PROFILE

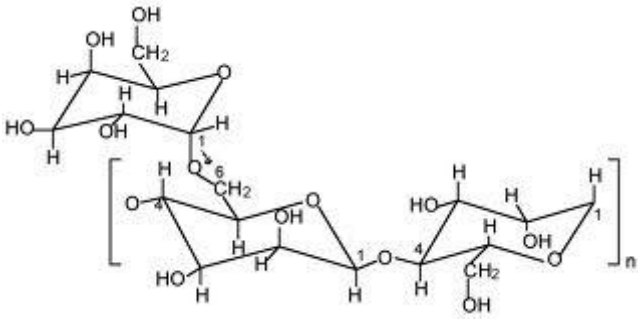
GuarGum

General Descriptions

Guar gum is a galactomannan, obtained from plant Cyamopsis tetragonolobus.

Description

Powder is whitish and yellowish consisting of slight odor. Guar gum is mainly consisting of the high molecular weight polysaccharides composed of galactomannans which are consisting of a linear chain of (1→4)-linked β-D-mannopyranosyl units with (1→6)-linked α-D-galactopyranosyl residues as side chains. The mannose: galactose ratio is approximately 2:1. The molecular weight range is 50,000-8,000,000.



Structural Formula.

Structure of Guar Gum

Functional categories

It has wide applications in Pharmaceutical formulations, Cosmetic, Food, Textile, Paper, Explosive, Toiletries industries etc. In Pharmaceuticals, it is used as tablet binder and disintegrate, suspending, thickening and stabilizing agent, as a controlled release carrier.

Solubility

Guar gum is more soluble than locust bean gum and is a better stabilizer, as it has more galactose branch points. Unlike locust bean gum, it is not self-gelling. However, either borax or calcium can cross-link guar gum, causing it to gel. In water, it is nonionic and hydro colloidal. It is not affected by ionic strength or pH, but will degrade at pH extremes at temperature (e.g. pH 3 at 50°C). It remains stable in solution over pH range 5-7. Strong acids cause hydrolysis and loss of viscosity and alkalies in strong concentration also tend to reduce viscosity. It is insoluble in most hydrocarbon solvents.

Viscosity (dynamic)

Guar gum shows high low-shear viscosity but is strongly shear-thinning. It is very thixotropic above 1% concentration, but below 0.3%, the thixotropy is slight. It has much greater low-shear viscosity than that of locust bean gum and also generally greater than that of other hydrocolloids. Guar gum shows viscosity synergy with xanthan gum. Guar gum and micellar casein mixtures can be slightly thixotropic if a biphase system forms.

Stability and Storage Condition

Aqueous guar gum dispersions have a buffering action and are stable at pH 4-10.5. The bacteriological stability of guar gum dispersion may be improved by addition of mixture of 0.15% methyl paraben and 0.02% propyl paraben as preservatives. It should be stored in well closed container in cool and dry place.

Gum Karaya

Synonyms

Karaya, gum karaya, Sterculia, gum sterculia, Kadaya, Katilo, Kullo, Kuterra.

Functional category

Emulsifier, stabilizer, thickening agent.

Applications in pharmaceutical formulations

Used in oral solid dosage formulations as an emulsifier, stabilizer and thickening agent.

Description

Ungrounded product: occurs in tears of variable size and in broken irregular pieces having a characteristic semi-crystalline appearance; pale yellow to pinkish brown; translucent and horny powdered product: pale grey to pinkish brown; a distinctive odour of acetic acid. Items of commerce may contain extraneous materials such as pieces of bark which must be removed before use in food.

Hydroxy Propyl Methyl Cellulose

General Descriptions

Nonproprietry Names

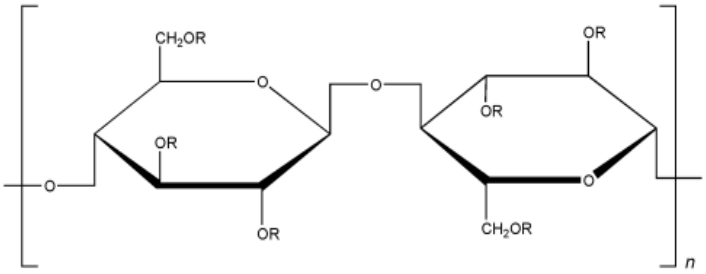
BP: Hypromellose, USP: Hypromellose.

Synonyms

Methocel, HPMC2208**,** Benecal MHPC, Pharmacoat.

Description

It is odorless & tasteless, white or creamy white colored Fibrous or granular powder.



Structural Formula.

Structure of HPMC

Functional categories

Tablet binder, Coating agent, Film former stabilizing agent, Suspending agent, Viscosity increasing agent.

Solubility

It is soluble in cold water but insoluble in Chloroform, ethanol (95%) & ether but Soluble in mixture of ethanol & dichloromethane mixture of methanol & dichloromethane, mixture of alcohol.

Viscosity (dynamic)

A wide range of viscosity types are commercially available. Aqueous solutions are most commonly prepared, although hypromellose may also be dissolved in aqueous alcohols such as ethanol and propan-2-ol provided the alcohol content is less than 50% w/w. Dichloromethane and ethanol mixtures may also be used to prepare viscous Hypromellos.

P^H: 5.5 – 8.0 for a 1 % w/w aqueous solution.

Melting point: Brown at 190- 200^{0}C; chars at 225-230^{0}C.

Specific gravity: 1.26

Loss on drying: < 5.0 %

Density (bulk): 0.341 gm/cm^3

Density (tapped): 0.557 gm/cm^3

Stability and storage Conditions

Hypromellose powder is a stable material although it is hydroscopic after drying. Solutions are stable at pH 3.Upon heating and cooling hypromellose undergoes a reversible gel transformation. Viscosity of solutions is reduced by increasing the temperature. Depending upon the grade and concentration of material, the gel point is 50-90°C. It is stable material although it is hygroscopic after drying. It should be stored in a well -closed container in a cool dry place.

Incompatibilities

Incompatible with some oxidizing Agents.

Application

It is widely used oral & topical pharmaceutical formulations primarily used in film-coating, binder in tablets in concentrations of 2 – 5%.

Carbomer (Carbopol)

Carbomer 934Pare the synthetic high-molecular-weight polymers of acrylic acid that are cross linked with either allyl sucrose or allyl ethers of pentaerythritol. They contain between 56% and 68% of carboxylic acid (-COOH) groups calculated on the dry bases. The viscosity of neutralized 0.5 percent aqueous dispersion of Carbomer 934P is between 29,400 and 39,400 cps.

Nonproprietary Names

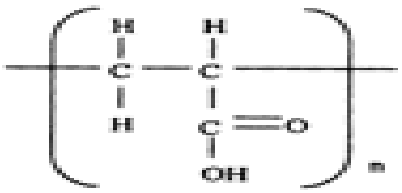
BP: Carbomers.

PhEur: Carbomera.

USPNF: Carbomer.

Synonyms

Acritamer; acrylic acid polymer; Carbopol; carboxypolymethylene, polyacrylic acid; carboxyvinyl polymer.



Structural Formula.

Carbomer polymers are formed from repeating units of acrylicacid. The monomer unit is shown above. The polymer chains are crosslinked with allyl sucrose or allylpentaerythritol.

Description

White, fluffy powder, it is having a slight characteristic odor.Is hygroscopic. The pH of 1 in 100 dispersion is about 3.

Solubility

When neutralized with alkali hydroxyls or with amines, it dissolves in water, in alcohol and in glycerin.

Functional Category

Bioadhesive, emulsifying agent, release-modifying agent, suspending Agent, tablet binder, viscosity-increasing agent.

Pharmaceutical Applications

- Carbomer are mainly used in liquid or semisolid pharmaceutical formulations and solid dosage forms as suspending or viscosity-increasing agents.
- Carbomer 934P, 971P, 974P may be used in oral preparations, in suspensions, tablets or sustain release tablet formulations.
- In tablet formulations, carbomers are used as dry or wet binders and as a rate controlling excipients.
- Carbomer resins have also been investigated in the preparation of sustained, release matrix beads, as enzyme inhibitors of intestinal proteases in peptide-containing dosage forms, in oral mucoadhesive controlled drug delivery system.
- Carbomers are also employed as emulsifying agents in the preparation of oil-in-water emulsions for external use.
- Carbomers are also used in cosmetics.

Packaging

Packaging in aluminum tubes usually requires the formulation to have a pH less than 6.5, and packaging other metallic tubes or containers necessitates a pH greater than 7.7 to prolong Carbomer stability.

Storage

Carbomer powder should be stored in an airtight, corrosion-resistant container in a cool, dry place. The use of glass, plastic or resin-linked containers is recommended for the storage of formulations containing Carbomer.

Microcrystalline Cellulose

Synonyms

Avicel PH; Celex; cellulose gel; Celphere; Ceolus KG; crystalline cellulose; E460; Emcocel; Ethispheres.

Chemical Name: Cellulose.

Empirical Formula: $(C_6H_{10}O_5)n$ where $n \approx 220$.

Molecular Weight: ≈36 000.

Functional Category: Adsorbent; suspending agent; tablet and capsule diluent; tablet disintegrant.

Applications

Microcrystalline cellulose is widely used in pharmaceuticals, primarily as a binder/diluent in oral tablet and capsule formulations where it is used in both wet-granulation and direct-compression processes. In addition to its use as a binder or diluent, microcrystalline cellulose also has some lubricant and disintegrant properties that make it useful in tableting. Microcrystalline cellulose is also used in cosmetics and food products.

TABLE: 1 Uses of microcrystalline cellulose.

Use	Concentration (%)
Adsorbent	20–90
Anti-adherent	5–20
Capsule binder/diluents	20–90
Tablet disintegrant	5–15
Tablet binder/diluents	20–90

Description

Microcrystalline cellulose is a purified, partially de polymerized cellulose that occurs as a white, odorless, tasteless, crystalline powder composed of porous particles. It is commercially available in different particle sizes and moisture grades that have different properties and application.

Angle of repose (θ): 34.4°.

Density (bulk): 0.337 g/cm^3 for Avicel P^H 200, 0.32 g/cm^3 for Avicel P^H 101.

Density (tapped): 0.478 g/cm^3 for Avicel 200 0.45 g/cm^3 for Avicel P^H-101.

Density (true): 1.512–1.668 g/cm^3.

Flow ability: 1.41 g/s

Melting point: 260–270°C.

Moisture content: Typically less than 5% w/w. microcrystalline cellulose is hygroscopic.

Particle size distribution: Typical mean particle size is 20–200 μm.

Solubility: Slightly soluble in 5% w/v sodium hydroxide solution; practically insoluble in water, dilute acids.

Specific surface area: 1.21–1.30 m^2/g forAvicel P^H-101 0.78–1.18 m^2/g for Avicel P^H-200.

Stability: Microcrystalline cellulose is a stable though hygroscopic material.

Storage Conditions: The bulk material should be stored in a well-closed container in a cool, dry place.

Safety: It is widely used in oral pharmaceutical formulations is generally regarded as a relatively nontoxic and nonirritant material. Deliberate abuse of formulations containing cellulose, either by inhalation or by injection, has resulted in the formation of cellulose granulomas.

Polyvinylpyrrolidone (PVP)

Synonyms

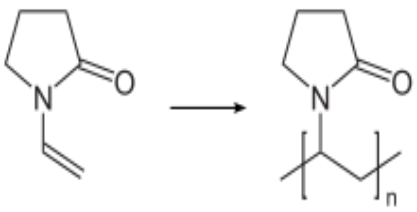
E1201; Kollidon; Plasdone; poly [1-(2-oxo-1 pyrolidinyl) ethylene] polyvidone; poly vinyl pyrrolidone; PVP; 1-vinyl-2-pyrrolidinone polymer.

Grades

PVP K-12, K-15, K-17, K-25, K-30, K-60, K-90, K-120.

Structure

Poly vinyl pyrrolidone (PVP) is a water-soluble polymer made from the monomer N-vinyl pyrrolidone.



Functional Category

Disintegrant; dissolution aid; suspending agent; tablet binder.

Description

It occurs as a fine, white to creamy-white colored, odorless or almost odorless, hygroscopic powder.

Melting point

Softens at 150°C.

Solubility

Freely soluble in acids, chloroform, ethanol (95%), ketones, methanol and water. practically insoluble in ether, hydrocarbons and mineral oil. In water, the concentration of a solution is limited only by the viscosity of the resulting solution, which is a function of the K-value.

Stability and Storage

Povidone darkens to some extent on heating at 150°C, with a reduction in aqueous solubility. It is stable to a short cycle of heat exposure around 110–130°C; steam sterilization of an aqueous solution does not alter its properties. Aqueous solutions are susceptible to mold growth and consequently require the addition of suitable preservatives.

It may be stored under ordinary conditions without undergoing decomposition or degradation. However, since the powder is hygroscopic, it should be stored in an airtight container in a cool, dry place.

Incompatibilities

It is compatible in solution with a wide range of inorganic salts, natural and synthetic resins, and other chemicals. It forms molecular adducts in solution with sulfathiazole, sodium salicylate, salicylic acid, phenobarbital, tannin and other compounds; the efficacy of some preservatives, e.g. thimerosal, may be adversely affected by the formation of complexes with povidone.

Safety

When consumed orally, povidone may be regarded as essentially nontoxic since it is not absorbed from the gastrointestinal tract or mucous membranes. It additionally has no irritant effect on the skin and causes no sensitization.

Uses

In tableting, povidone solutions (0.5-5% w/v) are used as binders in wet-granulation processes. It is also added to powder blends in the dry form and granulated *in situ* by the addition of water, alcohol, or hydroalcoholic solutions. It is used as a solubilizer in oral and parenteral formulations and has been shown to enhance dissolution of poorly soluble drugs from solid-dosage forms. Povidone solutions may also be used as coating agents.

5.6 Magnesium Stearate

Synonyms

Magnesium octadecanoate; octadecanoic acid, magnesium salt; stearic acid, magnesium salt.

Molecular weight: 591.34.

Structural formula: $[CH_3(CH_2)_{16}COO]_2Mg$.

Functional category: Tablet and capsule lubricant.

Applications in pharmaceutical formulation technology

It is primarily used as a lubricant in capsule and tablet manufacture at concentrations between 0.25 % and 5.0 % w/w.

Description

Magnesium stearate is a fine, white, precipitated or milled, impalpable powder of low bulk density, having a faint odor of stearic acid and a characteristic taste. The powder is greasy to touch and readily adheres to the skin.

Crystalline forms

High purity magnesium stearate has been isolated as a trihydrate, dihydrate and an anhydrate.

Flow ability

Poorly flowing, cohesive powder.

Melting range

117-150^{o}C (commercial samples) 126-130^{o}C (high purity magnesium stearate).

Solubility

Practically insoluble in ethanol, ethanol (95%), ether and water; slightly soluble in warm benzene and warm ethanol (95%).

Specific surface area: 1.6-14.8 m^2/g.

Density (bulk): 0.159 g/cm^3.

Density (tapped): 0.286 g/cm^3.

Density (true): 1.092 g/cm^3.

Stability and Storage Conditions

Magnesium stearate is stable and should be stored in a well-closed container in a cool, dry place.

Incompatibilities

Incompatible with strong acids, alkalis and iron salts strong oxidizing materials. Magnesium stearate cannot be used in products containing aspirin, some vitamins and most alkaloid salts.

Method of manufacture

Magnesium stearate is prepared either by the interaction of aqueous solutions of magnesium Chloride with sodium stearate or by the interaction of magnesium oxide, hydroxide or carbonate with stearic acid at elevated temperatures.

Safety

Magnesium stearate is widely used as a pharmaceutical excipient and is generally regarded as being nontoxic following oral administration. However, oral consumption of large quantities may result in some laxative effect or mucosal irritation.

Talc

Synonyms

Altaic; E553b; hydrous magnesium calcium silicate; hydrous magnesium silicate; Luzenac Pharma; magnesium hydrogen metasilicate; Magsil Osmanthus; Magsil Star; powdered talc; purified French chalk; Purtalc; soapstone; steatite; Superiore.

Functional category

Anticaking agent; Tablet and Capsule diluent; Tablet and Capsule lubricant.

Applications in pharmaceutical formulations

Used in oral solid dosage formulations as a lubricant and glidant (1-10%), Dissolution retardant in the development of controlled release products. Used as dusting powder (90.0-

99.0), Lubricant properties in cosmetics and food properties, Talc is widely used in oral solid dosage formulations as lubricant and diluents.

Description

Talc is a very fine, white to greyish-white coloured, odorless, impala table crystalline powder. It adheres to the skin readily. Insoluble in water, dilute acids, alkalis and organic solvents.

Moisture content

Talc absorbs insignificant amounts of water at 25°C and relative humidities up to about 90%.

Solubility

practically insoluble in dilute acids and alkalis, organic solvents and water.

Specific gravity: 2.7–2.8.

Specific surface area: 2.41–2.42 m^2/g.

Stability and storage conditions

Talc is a stable material and may be sterilized by heating at 160^0C for not less than 1 hr. It may also be sterilized by exposure to ethylene oxide or gamma irradiation. Talc should be stored in a well-closed container in a cool, dry place.

Incompatibilities

Talc is incompatible with quaternary ammonium compounds.

Method of manufacture

Talc is a naturally occurring hydropolysilicate mineral found in many parts of the world including: Australia; China; Italy and the US. Naturally occurring talc is mined and pulverized before being subjected to flotation processes to remove various impurities such as: asbestos (tremolite), carbon, dolomite, iron oxide and various other magnesium and carbonate minerals. Following this process the talc is finely powdered, treated with dilute Hydrochloric acid, washed with water and then dried. It is the processing variables of agglomerated talc that strongly influence its physical characteristics.

Safety

Talc is mainly used in tablet and capsule formulations. Following oral ingestion talc is not absorbed systemically and may thus be regarded as an essentially nontoxic material. However, intranasal or intravenous abuse of products containing talc can cause granulomas in body tissues, particularly the lungs. Contamination of wounds or body cavities with talc may also cause granulomas, hence it should not be used to dust surgical gloves. Inhalation of talc causes irritation and may cause severe respiratory distress in infants. Although talc has been extensively investigated for its carcinogenic potential with some suggestion that there is an increased risk of ovarian cancer in women using talc, the evidence is inconclusive. However, talc contaminated with asbestos has been concluded to be carcinogenic in humans and asbestos-free grades should therefore be used in pharmaceutical products. Also, long-term toxic effects of talc contaminated with large quantities of Hexachlorophene caused serious irreversible neurotoxicity in infants accidentally exposed.

Handling precautions

Observe normal precautions appropriate to the circumstances and quantity of material. Talc is irritant if handled and prolonged excessive exposure may cause pneumoconiosis. Eye protection, gloves and a respirator are recommended.

METHODOLOGY

Analytical method development

Determination of absorption maxima

100mg of Etodolac pure drug was dissolved in 100ml of 0.1N HCl (stock solution-I). 10ml of solution was taken from the stock solution-I and make up with100ml of 0.1N HCl (Stock solution-II i.e100µg/ml). From stock solution II, 10ml was taken and make up with 100 ml of 0.1N HCl (10µg/ml). The solution was scanned in the range of 200 – 400.

Preparation calibration curve

100mg of Etodolac pure drug was dissolved in 100ml of 0.1N HCl (stock solution-I). From the stock solution-I, 10ml of solution was taken and make up with100ml of 0.1N HCl (Stock solution-II, 100µg/ml). From this take 0.5, 1, 1.5, 2 and 2.5 ml of solution and make up to 10ml with 0.1N HCl to obtain 5, 10, 15, 20 and 25µg/ml of Etodolac per ml of solution. The absorbance of the above dilutions were measured at 279 nm using UV-Spectrophotometer taking 0.1N HCl as blank. Thegraph was plotted by taking Concentration on X-Axis and absorbance on Y-Axis which gives a straight line. The Linearity of standard curve was

assessed from the square of correlation coefficient (R^2) which determined by least-square linear regression analysis. The above procedure was repeated with pH 6.8 phosphate buffer.

Preformulation Studies

Drug and excipient compatibility studies

Fourier Transform Infrared (FTIR) spectroscopy

Drug excipient interaction studies are significant for the successful formulation of every dosage form. Fourier Transform Infrared (FTIR) Spectroscopy studies were used for the assessment of physicochemical compatibility and interactions, which helps in the prediction of interaction between drug and other excipients. In the current study 1:1 ratio was used for preparation of physical mixtures used for analyzing of compatibility studies. FT-IR studies were carried out with a Bruker FTIR facility using KBr pellet.

Formulation and Evaluation

Preparation of tablets

Tablets of Etodolac were prepared by direct compression method using Guar gum, HPMC K15 M and gum karaya, carbopoland microcrystalline cellulose as diluents and talc and magnesium stearate as glidant and lubricant.

Procedure

Drug and all other ingredients were individually passed through sieve no ≠ 60.

First the drug and polymers should be mixed uniformly with diluents using mortar and pestle. Add talc and magnesium stearate to powder blend by physical mixing and were compressed into tablets using lab press rotary tablet punching machine.

Table No: 2 Formulation of Etodolac mucoadhesive tablets.

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Etodolac	200	200	200	200	200	200	200	200	200
Guar gum	50	100	150	-	-	-	-	-	-
Gum karaya	-	-	-	50	100	150	-	-	-
HPMC K15 M	-	-	-	-	-	-	50	100	150
Carbopol	100	100	100	100	100	100	100	100	100
Mg.stearate	5	5	5	5	5	5	5	5	5
Talc	5	5	5	5	5	5	5	5	5
MCC	190	90	40	190	90	40	190	90	40
Tablet weight	500	500	500	500	500	500	500	500	500

Evaluation Parameters

Pre Compression parameters

Bulk density (D_B)

Bulk density is the ratio between a given mass of the powder and its bulk volume.

Bulk density = Mass of Powder/Bulk volume of the powder

Bulk density (D_B) = W /V_0

Procedure

An accurately weighed quantity of granules (w) (which was previously passed through sieve No: 40) was carefully transferred into 250 ml measuring cylinder and measure the bulk volume.

Tapped Density (D_T)

Tapped density [104] is the ratio between a given mass of powder (or) granules and the constant (or) fixed volume of powder or granules after tapping.

Tapped density = mass of the powder/ tapped volume.

Procedure

An accurately weighed quantity of granules (w) (which was previously passed through sieve No: 40) was carefully transferred into 250 ml measuring cylinder and the cylinder was tapped on a wooden surface from the height of 2.5 cm at two second intervals. The tapping was continued until no further change in volume (until a constant volume) was obtained (V_f). The tapped density was calculated by using the formula.

Tapped density (D_T) = W/V_f.

Hausner's ratio

Hausner's ratio is an indirect index of ease of powder flow and was calculated by the formula.

Hausner'sratio = D_T/D_B.

Where, D_T is the tapped density.

D_B is the bulk density.

Compressibility index

Compressibility index (CI) was determined by measuring the initial volume (V_o) and final volume (V_f) after hundred tapping's of a sample in a measuring cylinder. It indicates the powder flow properties and expressed in terms of percentage and given in table no. 14 and calculated by using the formula.

% Compressibility index = V_o - V/V_o x 100.

Angle of repose

Angle of repose was measured by fixed funnel method. It determines flow property of the powder. It is defined as maximum angle formed between the surface of the pile of powder and the horizontal plane.

The powder was allowed to flow through the funnel fixed to a stand at definite height (h). By measuring the height and radius of the heap of powder formed (r), angle of repose was calculated by using formula given below and the calculated values obtained was shown in table no. 2.

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

Where, θ is the angle of repose.

h is the height in cm.

r is the radius in cm.

Flow property

Table No: 3 The flow property of powder blend.

Flow property	Angle of repose	Compressibility index (%)	Hausner's ratio
Excellent	25-30	<10	1.00-1.11
Good	31-35	11-15	1.12-1.18
Fair	36-40	16-20	1.19-1.25
Passable	41-45	21-25	1.26-1.34
Poor	46-55	26-31	1.35-1.45
Very Poor	56-65	32-37	1.46-1.59
Very Very Poor	>66	>38	>1.60

Post Compression parameters

Weight variation test

Twenty tablets were randomly selected and weighed, to estimate the average weight and that were compared with individual tablet weight. The percentage weight variation was calculated

as per Indian Pharmacopoeiaspecification. Tablets with an average weight above 250 mg so the % deviation was ± 5 %.

IP standards of uniformity of weight.

S. No.	Average weight of tablet	% of deviation
1	≤ 80 mg	10
2	> 80 mg to <250 mg	7.5
3	≥ 250 mg	5

Friability test

Twenty tablets were weighed and subjected to drum of friability test apparatus. The drum rotated at a speed of 25 rpm. The friabilator was operated for 4 minutes and reweighed the tablets. % loss (F) was calculated by the following formula.

$F = 100 (W_o - W)/W_o$.

Where W_o= Initial weight, W = Final weight.

Hardness test

The hardness of tablets was measured by using Monsanto hardness tester. The results were complies with IP specification.

Thickness test

The rule of physical dimension of the tablets such as sizes and thickness is necessary for consumer acceptance and maintain tablet uniformity. The dimensional specifications were measured by using screw gauge. The thickness of the tablet is mostly related to the tablet hardness can be used as initial control parameter.

Drug content

The amount of drug in tablet was important for to monitor from tablet to tablet and batch to batch is to evaluate for efficacy of tablets. For this test, take ten tablets from each batch were weighed and powdered. Weighed equivalent to the average weight of the tablet powder and transferred into a 100 ml volumetric flask and dissolved in a suitable quantity of media. The solution was made up to the mark and mixed well. Then filter the solution. A portion of the filtrate sample was analyzed by UV spectrophotometer.

***In vitro* drug release studies**

Dissolution parameters

Apparatus-- USP-II, Paddle Method.

Dissolution Medium-- 0.1 N HCl, pH 6.8 Phosphate buffer.

RPM-- 50.

Sampling intervals (hrs)-- 1,2,3,4,5,6,7,8,10,11 and 12.

Temperature-- 37°c ± 0.5°c.

Procedure

900ml 0f 0.1 HCl was placed in vessel and the USP apparatus –II (Paddle Method) was assembled. The media was allowed to equilibrate to temp of 37°c ± 0.5°c. Tablet was placed in the vessel and apparatus was operated for 2 hours. Then 0.1 N HCl was replaced with pH 6.8 phosphate buffer and process was continued up to 12 hrs at 50 rpm. At specific time intervals, withdrawn 5 ml of sample and again 5ml media was added to maintain the sink condition. Withdrawn samples were analyzed at wavelength of drug using UV-spectrophotometer.

***In vitro* mucoadhesion studies**

The mucoadhesive strength of the tablets was measured on modified physical balance. The goat mucus membrane was used as model membrane and pH 1.2 solutions were used as the moistening fluid. The goat stomach mucosa was placed in tyrode solution at 37^0c for 2 hours. The original mucus membrane was separated and washed thoroughly with pH 1.2 buffer solutions then it was tied to Teflon coated glass slide and it was fixed above the protrusion in the Teflon block. The block was kept in a beaker (containing pH1.2 solution) that just touches the membrane for moisten the membrane. Placed 5g of weight on the right side of the pan and balanced two sides. The beaker with Teflon block was kept below the left hand of balance. The tablet was stuck on to the lower side of the left hand side pan. Then remove the 5g weight from the right pan. This lowered the left pan along with the tablet over the membrane with the weight of 5g. this was kept for 3 mins. Then the weight on the right hand side was added in an increment of 0.5 g until the tablet separate from the membrane surface. The excess weight on the right pan i.e total weight minus 5g was taken as the measure of the mucoadhesive strength from the mucoadhesive strength, the force of adhesion was calculated by using following formula.

Force of adhesion (N) = Mucoadhesive strength/100 × 9.81.

Application of Release Rate Kinetics to Dissolution Data

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 were fitted into zero-order, first order, Higuchi and Korsmeyer-Peppas release model.

Zero order release rate kinetics

To study the zero–order release kinetics the release rate data ar e fitted to the following equation.

$F = K_o t$.

Where, 'F' is the drug release at time't' and 'K_o' is the zero order release rate constant. The plot of % drug release versus time is linear.

First order release rate kinetics

The release rate data are fitted to the following equation.

Log (100-F) = kt.

A plot of log cumulative percent of drug remaining to be released vs. time is plotted then it gives first order release.

Higuchi release model

To study the Higuchi release kinetics, the release rate data were fitted to the following equation.

F = k t1/2.

Where, 'k' is the Higuchi constant.

In higuchi model, a plot of % drug release versus square root of time is linear.

Korsmeyer and Peppas release model

The mechanism of drug release was evaluated by plotting the log percentage of drug released versus log time according to Korsmeyer- Peppas equation. The exponent 'n' indicates the mechanism of drug release calculated through the slope of the straight Line.

$M_t / M_\infty = K t^n$.

Where, M_T / M_∞ is fraction of drug released at time 't', k represents a constant and 'n' is the diffusional exponent, which characterizes the type of release mechanism during the

dissolution process. For non-Fickian release, the value of n falls between 0.5 and 1.0; while in case of Fickian diffusion, n = 0.5; for zero-order release (case I I transport), n=1; and for super case II transport, n > 1.In this model, a plot of log (M_t/ M_∞) versus log (time) is linear.

RESULTS AND DISCUSSION

The present work was designed to developing mucoadhesive tablets of Etodolac using various polymers. All the formulations were evaluated for physicochemical properties and *in vitro* drug release studies.

Analytical Method

Standard graph of Etodolac in 0.1N HCl

The scanning of the 10µg/ml solution of Etodolac in the ultraviolet range (200-400nm) against 0.1 N HCl blank gave the λ_{max} as 279 nm. The standard concentrations of Etodolac (5-25µg/ml) prepared in 0.1N HCl showed good linearity with R^2 value of 0.999, which suggests that it obeys the Beer-Lamberts law.

Table No 4: Standard curve forEtodolac in 0.1N HCl.

Concentration (µg ml)	Absorbance ± % RSD
0	0
5	0.136 ± 0.151
10	0.245 ± 0.098
15	0.361 ± 0.135
20	0.472 ± 0.146
25	0.589 ± 0.085

(n=6) Values (Absorbance ± %RSD).

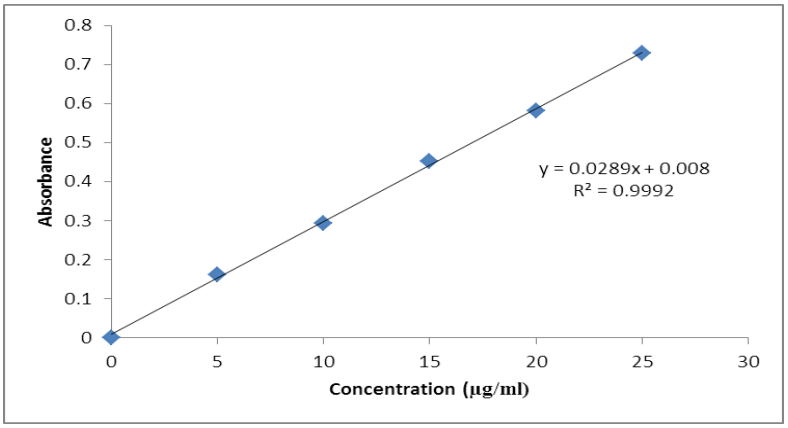


Fig. 1: Calibration curve forEtodolac in 0.1 N HCl at 279 nm.

Standard Curve of Etodolac in Phosphate buffer pH 6.8

The scanning of the 10µg/ml solution of Etodolac in the ultraviolet range (200-400nm) against 6.8 pH phosphate buffer as blank gave the λ_{max} as 276 nm. The standard concentrations of Etodolac (5-25µg/ml) prepared in 6.8 pH phosphate buffer showed good linearity with R^2 value of 0.999, which suggests that it obeys the Beer-Lamberts law.

Table 5: Standard curve of Etodolac in Phosphate buffer pH 6.8.

Concentration (µg/ml)	Absorbance± % R.S.D.
0	0
2	0.168 ± 0.18
4	0.293 ± 0.168
6	0.451 ± 0.141
8	0.582 ± 0.161
10	0.728 ± 0.106

(n=6) Values (Absorbance ± % RSD).

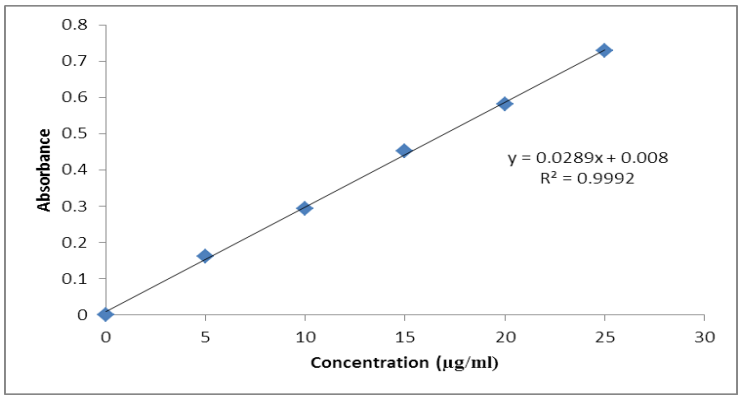


Fig 2: Calibration of Etodolac in Phosphate buffer pH 6.8 at 276nm.

DRUG AND EXCIPIENT COMPATIBILITY STUDIES

FTIR study

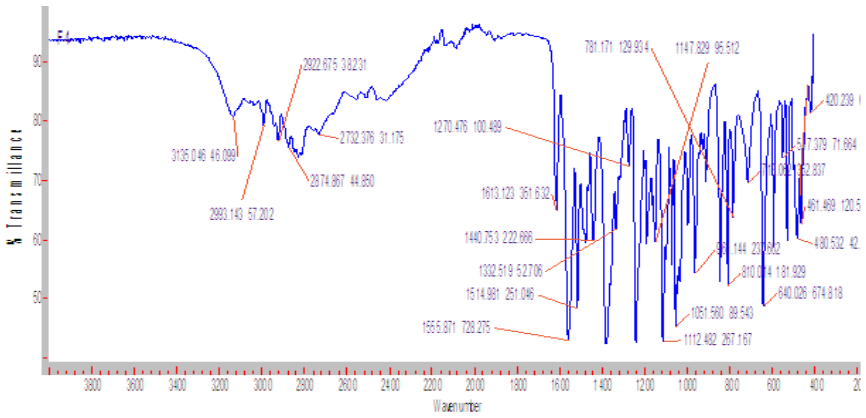


Figure 3: FTIR spectrum of Etodolac.

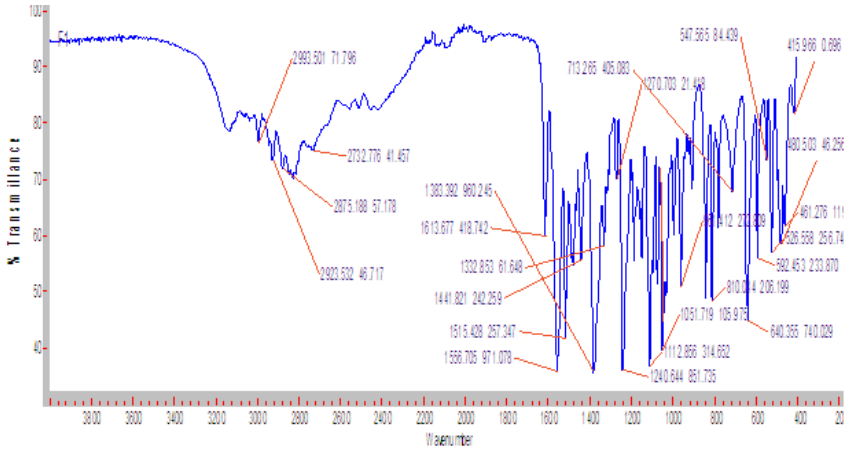


Figure 4: FTIR of optimizedEtodolac formulation.

From the above FTIR graphs showed no interaction between drug and excipients, it indicates good compatibility between drug and polymers.

Evaluation Parameters

Pre-compression parameters

Table 6: Pre compression parameters of Etodolac powder blend.

Formulation Code	Angle of Repose	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's Ratio
F1	24.11 ± 0.11	0.47 ± 0.05	0.53 ± 0.057	11.32 ± 0.58	1.12 ± 0.015
F2	26.67 ± 0.57	0.45 ± 0.057	0.56 ± 0.015	16.07 ± 0.47	1.24 ± 0.015
F3	26.54 ± 0.57	0.52 ± 0.01	0.60 ± 0.051	13.33 ± 0.57	1.15 ± 0.012
F4	24.43 ± 0.63	0.55 ± 0.015	0.62 ± 0.057	11.29 ± 0.15	1.12 ± 0.012
F5	27.34 ± 0.58	0.47 ± 0.05	0.56 ± 0.015	12.50 ± 0.21	1.19 ± 0.005
F6	26.22 ± 0.51	0.56 ± 0.015	0.63 ± 0.011	11.11 ± 0.35	1.12 ± 0.012
F7	25.18 ± 0.56	0.49 ± 0.02	0.58 ± 0.01	15.51 ± 0.42	1.18 ± 0.011
F8	27.22 ± 0.56	0.57 ± 0.055	0.66 ± 0.017	13.63 ± 0.57	1.15 ± 0.013
F9	26.15 ± 0.41	0.54 ± 0.041	0.62 ± 0.011	12.90 ± 0.43	1.14 ± 0.011

Tablet powder blend was subjected to various pre-compression parameters. The angle of repose values was showed from 20 to 30; it indicates that the powder blend has good flow properties. The bulk density of all the formulations was found to be in the range of 0.45±0.057 to 0.57±0.055 (gm/cm^3) showing that the powder has good flow properties. The tapped density of all the formulations was found to be in the range of 0.53±0.057 to 0.66±0.017 showing the powder has good flow properties. The compressibility index of all the formulations was found to be ranging from 11 to 16 which showed that the powder has good flow properties. All the formulations were showed the Hausner's ratio ranging from 0 to 1.25 indicating the powder has good flow properties.

Quality Control Parameters For tablets

Table 7: Post Compression Parameters of Etodolactablets.

Formulation codes	Weight variation (mg)	Hardness (kg/cm2)	Friability (%loss)	Thickness (mm)	Drug content (%)
F1	498.95 ±1.15	4.4 ± 0.11	0.45 ±0.015	5.12 ± 0.1	98.3 ± 0.1
F2	499.15 ±1.25	4.7 ± 0.15	0.54 ± .015	5.15 ±0.057	99.3 ± 0.15
F3	500.26 ±0.81	4.5 ± 0.27	0.55 ± 0.02	5.20 ± 0.057	98.2 ± 0.15
F4	505.36 ±1.17	4.6 ± 0.24	0.56 ± 0.03	5.21 ± 0.1	99.2 ± 0.1
F5	497.25 ±2.02	4.8 ± 0.19	0.48 ± 0.05	5.15 ± 0.057	99.3 ± 015
F6	496.26 ± .25	4.7 ± 0.21	0.45 ±0.015	5.21 ± 0.11	97.2 ± 0.1
F7	502.5 ± 1.15	4.6 ± 0.24	0.51± 0.01	5.25 ± 0.1	98.3 ± 0.2
F8	503.63 ±1.64	4.8 ± 0.10	0.52 ± .015	5.31± 0.1	99.5 ± 0.15
F9	500.31 ±1.52	4.6 ± 0.21	0.53±0.011	5.14±0.1	98.5 ± 0.15

Weight variation and thickness

All the formulations were evaluated for uniformity of weight using electronic weighing balance and the results are shown in table 7.4. The average tablet weight of all the formulations was found to be between 496.26±2.25 to505.36±1.17**.** The maximum allowed percentage weight variation for tablets weighing >250 mg is 5% and no formulations are not exceeding this limit. Thus all the formulations were found to comply with the standards given in I.P. And thickness of all the formulations was also complying with the standards that were found to be between 5.1 ± 0.057 to 5.31 ± 0.1.

Hardness and friability

All the formulations were evaluated for their hardness, using Monsanto hardness tester and the results are shown in table 7.4. The average hardness for all the formulations was found to be between **(4.4**±0.11**to4.8** ±0.19**) Kg/cm^2** which was found to be acceptable.

Friability was determined to estimate the ability of the tablets to withstand the abrasion during packing, handling and transporting. All the formulations were evaluated for their percentage friability using Roche friabilator and the results were shown in table 7.4. The average percentage friability for all the formulations was between 0.45 ± 0.015 and 0.56±0.03, which was found to be within the limit.

Drug content

All the formulations were evaluated for drug content according to the procedure described in methodology section and the results were shown in table 7.4. The drug content values for all the formulations were found to be in the range of (97.2 ± 0.1 to 99.5 ± 0.15)**.** According to IP

standards the tablets must contain not less than 95% and not more than 105% of the stated amount of the drug. Thus, all the formulations comply with the standards given in IP.

Swelling Index

All the formulations were evaluated for the swelling index. The water absorption increases with increase in concentration of hydrophilic polymer in the formulation and time duration. Among the all the formulation F6 formulation containing gum karaya showed 19.24 ± 1.35 to 86.47 ± 2.08 up to 12 hours and F9 formulation containing HPMC K15M showed 16.75 ± 1.47 to 82.47 ± 1.58. Swelling of natural gum plays important role in both Mucoadhesive property and release retardant activity. The mucoadhesive strength increased by raising polymer concentration due to extensive swelling of the gum in the interpenetration of polymeric chains with the mucin presents on the gastric mucosa. Swelling of the polymer stands vital for the development of matrix for retarding the release of drug from the formulation.

Table No 8: Swelling index of mucoadhesive Etodolac tablets.

Time (hr)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	10.25 ±1.02	13.54 ± 1.15	17.24 ± 1.23	11.15 ± 1.05	15.05 ± 1.32	19.24 ± 1.35	10.53 ± 1.61	14.42 ± 1.36	16.75 ± 1.47
2	16.47 ± 1.52	17.41 ± 1.28	22.42 ±1.35	14.32 ±1.15	19.42 ± 1.24	25.18 ± 0.95	16.48 ± 1.43	19.56 ± 1.25	22.85 ± 1.85
3	21.48 ± 1.36	21.80 ± 1.34	29.28 ±1.42	20.14 ± 1.34	23.31 ± 1.61	31.43 ± 1.48	21.72 ± 1.15	25.61 ± 1.46	28.14 ± 1.08
4	26.64 ± 1.42	26.46 ± 0.96	34.13 ±1.18	24.05 ± 1.05	27.52 ± 1.52	39.61 ± 1.31	25.35 ± 1.35	30.42 ± 1.55	33.46 ± 2.08
5	31.41 ± 0.95	30.23 ± 0.85	39.05 ±1.09	29.15 ± 1.15	31.43 ± 1.42	45.73 ± 1.26	31.15 ± 1.43	34.15 ± 1.31	39.51 ± 1.34
6	36.09 ± 1.16	35.36 ±1.08	43.16 ± 2.04	33.08 ± 1.23	35.18 ± 1.37	52.15 ± 1.43	37.69 ± 0.81	39.08 ± 1.61	46.07 ± 1.87
7	40.04 ± 1.08	41.05 ± 1.14	48.47 ±1.43	37.72 ± 1.34	39.09 ±1.23	59.26 ± 0.95	43.51 ± 1.06	44.43 ± 0.92	51.23 ± 1.43
8	44.41 ± 2.04	45.32 ± 1.62	52.51 ± 1.15	41.14 ± 1.51	44.11 ±1.16	65.41 ± 1.14	47.04 ± 1.19	49.82 ± 1.13	56.42 ±1.76
9	49.36 ± 1.56	51.27 ± 1.57	57.71 ± 1.57	46.63 ± 1.54	48.86 ± 1.27	71.85 ± 2.05	51.24 ± 1.57	53.17 ± 2.08	62.51 ±1.85
10	54.04 ± 1.47	55.74 ± 1.58	61.72 ± 2.04	51.47 ± 2.16	53.43 ± 1.51	75.64 ± 1.81	54.08 ± 2.04	57.63 ± 1.58	69.75 ±2.05
11	59.41 ± 1.33	60.04 ± 1.73	64.17 ± 1.85	54.28 ± 1.87	58.65 ± 1.76	80.08 ± 1.54	59.65 ± 2.14	62.78 ± 1.31	76.43 ±1.64
12	59.12 ± 2.04	60.74 ± 2.01	67.48 ± 1.56	54.07 ± 1.05	64.31 ± 1.41	86.47 ± 2.08	59.34 ± 1.41	68.07 ± 2.04	82.47 ± 1.58

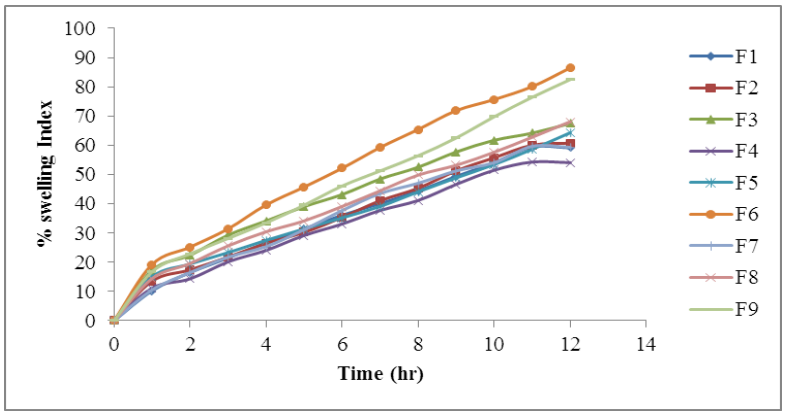


Figure: 5% Swelling index of mucoadhesive Etodolac tablets.

In Vitro Drug Release Studies

The formulations prepared with different natural polymers by wet granulation method. The tablets dissolution study was carried out in paddle dissolution apparatus using 0.1N HCL for 2 hours and 6.8 pH phosphate buffer for remaining hours as a dissolution medium.

Table 9: Dissolution Data of Etodolac Tablets Prepared with Guar gum in Different Concentrations

Time *(hr)*	Cumulative Percent Drug Released		
	F1	F2	F3
0	0	0	0
0.5	15.82±1.05	10.51±0.98	7.46±1.51
1	25.35±1.12	19.72±0.58	16.81±0.85
2	47.81±1.51	30.84±1.24	27.54±1.54
3	64.71±0.99	45.55±2.05	38.48±0.65
4	88.89±1.52	57.08±1.25	49.34±1.71
5	97.78±0.57	70.46±1.85	60.47±0.99
6	97.45±0.85	86.38±2.57	71.52±1.85
7		99.08±1.72	82.45±2.16
8			99.30±1.95

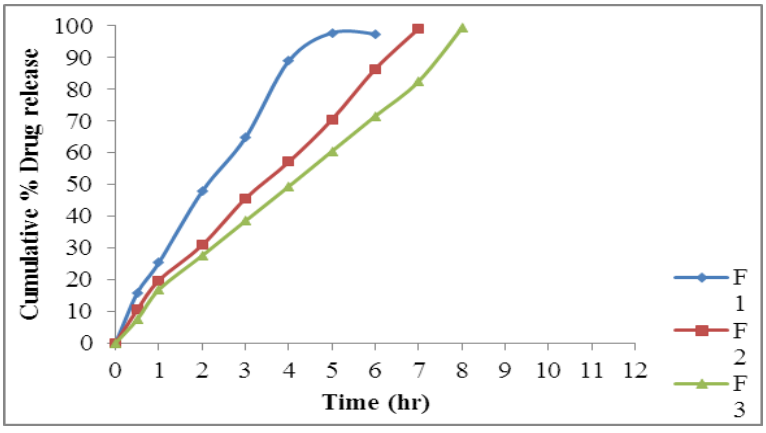


Figure 6: Dissolution study of Etodolac mucoadhesive tablets (F1 to F3).

The % drug release of formulations (F1 to F3) prepared with guar gum depends on the concentration of polymer. The concentration of guar gum 10% was unable to retard the drug release up to desired time. When the concnetration of polymer increased to 20% was unable to retard the drug up to 8 hours. In F3 formulation 30% of polymer concentration was used, showed maximum % drug release up to 8 hours i.e., 94.30%. Hence the guar gum polymer was not having good retardation property with drug. So these polymers were not considered as good formulations.

Table 10: Dissolution Data of Etodolac Tablets Prepared With Guar karaya In Different Concentrations.

Time (Hr)	Cumulative Percent Drug Released		
	F4	F5	F6
0	0	0	0
0.5	14.32±1.24	10.42±2.06	6.25 ± 1.34
1	33.69±2.01	25.14±1.65	11.24 ± 0.96
2	55.71±1.35	36.63±1.82	20.52 ± 1.04
3	77.22±0.95	49.39±0.98	29.54 ± 2.41
4	99.84±1.27	57.16±1.43	37.45 ± 1.86
5		66.92±1.27	45.85 ± 1.52
6		75.19±1.95	52.47 ± 2.06
7		86.34±1.45	60.26 ± 1.85
8		98.45±2.01	69.18 ± 2.11
9		98.51±1.12	76.15 ± 1.67
10			82.24 ± 1.24
11			91.05 ± 1.07
12			99.54 ± 2.13

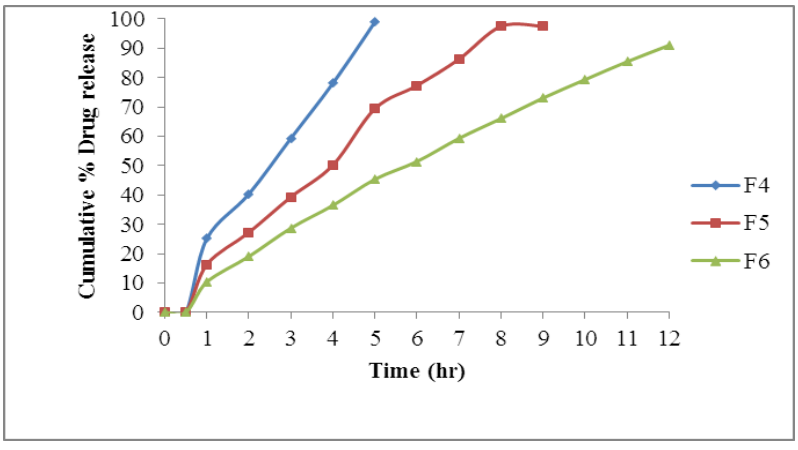


Figure 7: Dissolution study of Etodolac mucoadhesive tablets (F4 to F6).

The % drug release of F4 to F6 formulations depends on concentration of polymer in the formulation. The concentration of polymer 10% was unable to retard the drug release up to

desired time. When the concentration of 20% polymer was retard the drug i.e. 98.51±1.12 at 9 hours. In F6 formulations polymer concentration 30% showed good retardation, the maximum amount of drug release was up to desired time period i.e. 99.54 ± 2.13% at 12 hours. Among all the 3 formulation F6 formulation showed good release up to 12 hours.

Table 11: Dissolution Data of Etodolac Tablets Prepared with HPMC K15M in Different Concentrations.

Time (Hr)	Cumulative Percent Drug Release		
	F7	F8	F9
0	0	0	0
0.5	25.13 ± 1.09	16.32 ± 1.82	10.34 ± 1.41
1	40.34 ± 1.85	27.24 ±1.34	19.05 ± 0.87
2	59.34 ± 2.01	39.34 ±2.12	28.72 ± 1.34
3	78.13 ± 1.15	50.21 ± 0.99	36.47 ± 2.11
4	99.01 ± 2.08	69.43 ± 1.36	45.38 ± 1.42
5		77.32 ± 1.11	51.42 ± 1.41
6		88.34 ±1.63	59.32 ± 1.85
7		99.52 ± 1.45	66.07 ± 1.34
8		99.46 ± 2.01	73.08 ± 1.51
9			79.34 ± 1.24
10			85.47 ± 2.15
11			91.05 ± 2.03
12			99.03 ± 1.85

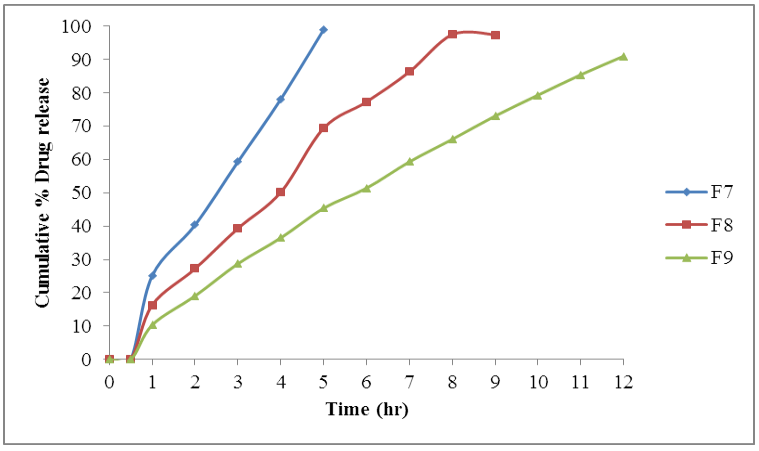


Figure 8: Dissolution study of Etodolac mucoadhesive tablets (F7 to F9).

The % drug release of F7 to F9 formulations depends on concentration of HPMC K15 M polymer in the formulation. The concentration of polymer 10% used in the formulation was unable to retard the drug release up to desired time. When increase the polymer concentration to 20%, it was retard the drug i.e. 99.46 ± 2.01 at 8 hours. In F9 formulations, the polymer concentration increase to 30% showed good retardation, the maximum amount of drug

release was up to desired time i.e. 99.54 ± 2.13% at 12 hours. Among all the 3 formulation F9 formulation showed good release up to 12 hours.

Hence based on dissolution data of 9 formulations, F6 and F9 formulations were showed better release up to 12 hours. It indicates increasing the concentration of polymer showing increase the viscosity of polymer so it decreases drug release and it prolonged up to 12 hours.

From the all the above in vitro evaluation parameters F6 formulation showed good results it has maximum drug release up to 12 hr due to it has good swelling index capacity. This is an optimized formulation (F6), it was further subjected to in vitro mucoadhesive strength and release kinetics.

Mucoadhesive strength

It was measuredfor the selected formulations**.** From this two parameters such as peak detachment force (N) and work of adhesion were calculated and they were found to be good for the formulation F6.

Formulation code	Mucoadhesion strength	
	Peak detachment force (N)	Work of adhesion (mJ)
F6	4.3	16.83

APPLICATION OF RELEASE RATE KINETICS TO DISSOLUTION DATA

Data of *in vitro* release studies of formulations which were showing better drug release were fit into different equations to explain the release kinetics of Etodolac release from mucoadhesive tablets. The data was fitted into various kinetic models such as zero, first order kinetics; higuchi and korsmeyer peppas mechanisms and the results were shown in below table

Table 12: Release kinetics data for optimized formulation (F6).

Cumulative (%) Release Q	Time (t)	Root (T)	Log (%) Release	Log (T)	Log (%) Remain
0	0	0			2.000
6.25	0.5	0.707	0.796	-0.301	1.972
11.24	1	1.000	1.051	0.000	1.948
20.52	2	1.414	1.312	0.301	1.900
29.54	3	1.732	1.470	0.477	1.848
37.45	4	2.000	1.573	0.602	1.796
45.85	5	2.236	1.661	0.699	1.734
52.47	6	2.449	1.720	0.778	1.677
60.26	7	2.646	1.780	0.845	1.599

69.18	8	2.828	1.840	0.903	1.489
76.15	9	3.000	1.882	0.954	1.377
82.24	10	3.162	1.915	1.000	1.249
91.05	11	3.317	1.959	1.041	0.952
99.54	12	3.464	1.998	1.079	-0.337

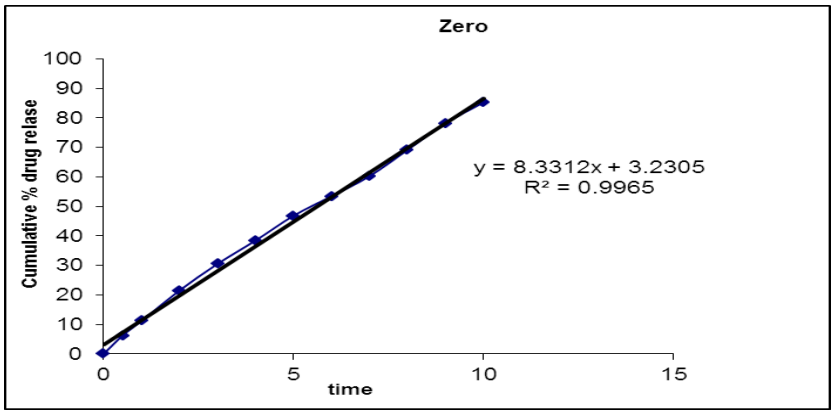


Figure 9: Graph of zero order kinetics.

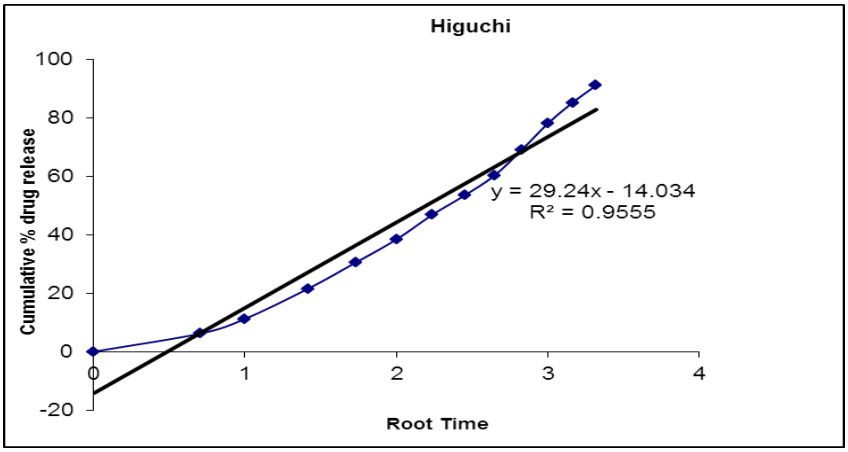


Figure 10: Graph of Higuchi release kinetics.

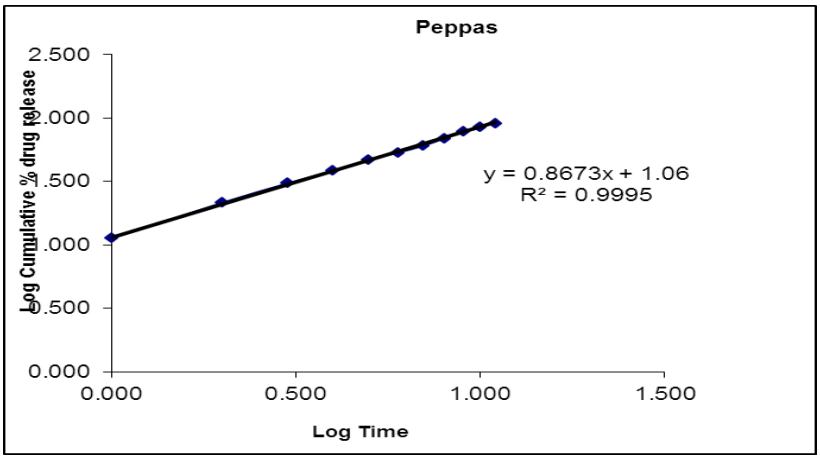


Figure 11: Graph of Peppas release kinetics.

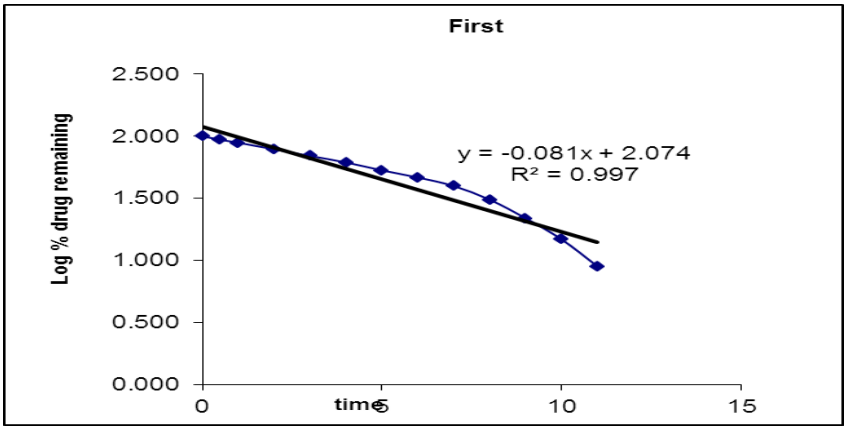


Figure 12: Graph for first order release kinetics.

Based on data the optimized formulation followed First order and Peppas release kinetics, non Fickian model (n=0.867).

CONCLUSION

Development of mucoadhesive Etodolac tablets is one of the dosage form will serve both the purposes of sustain release and presence of dosage form at the site of absorption.

Mucoadhesive tablets of Etodolac were prepared by direct compression method using various bioadhesive polymers like Guar gum, gumkaraya and HPMC K15M in different concentration.

The formulated mucoadhesive tablets were evaluated for different parameters such as drug excipient compatibility studies, weight variation, thickness, hardness, content uniformity, *In vitro* drug release and *In-vitro* mucoadhesive strength. *In- vitro* drug release studies performed in pH 1.2 and phosphate buffer pH 6.8 for 12hrs in standard dissolution apparatus. The data was subjected to zero order, first order, Zero and First diffusion models.

The following conclusions could be drawn from the results of various experiments.

FTIR studies concluded that there was no interaction between drug and excipients.

The physico-chemical properties of all the formulations prepared with different polymers like Guar gum, gum karaya and HPMC K15M were shown to be within limits.

Properties and from the results, it was concluded that the *in vitro* drug release, *in vitro* mucoadhesive strength of the optimized formulations is suitable for mucoadhesive delivery.

In-vitro drug release studies demonstrated the suitability of developed formulations for the release of Etodolac.

The present study concludes that mucoadhesive delivery of Etodolac tablets can be a good way to presence of drug at the site of absorption and to prolong duration of action of drug by reducing the frequency of dosing of Etodolac. The optimised formulation was found to be F6 formulation and its followed peppas release kinetics.

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