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Modification of natural hydrocolloid as disintegrant in aceclofenac tablet formulation

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Abstract

The purpose of present exploration was to modify kappa (k)-Carrageenan, by crosslinking, and assessed it as a tablet disintegrant to strengthen the solubility of the drug (aceclofenac) in tablet formulation. Modified k-Carrageenan was synthesized by reacting it with epichlorhydrin at heterogenous conditions. The swelling action of the product was investigated in order to optimize reaction circumstances for chemical cross-linking. Best modified k-Carrageenan procured by optimizing the reaction conditions and it was characterized for swelling index, particle size distribution, solubility, viscosity, gel strength and Fourier transform infrared spectroscopy (FTIR). Influence of modified k-Carrageenan on dissolution profile of therapeutic was also investigated along with other evaluation parameters. Modified k-Carrageenan exhibiting significant swelling index which is comparable to that of superdisintegrants. On comparative investigation as a tablet disintegrant by preparing anhydrous dicalcium phosphate tablet, modified k-Carrageenan showed disintegration time less than 20 seconds. Dissolution of aceclofenac (Class II) tablet formulaion utilizing modified k-Carrageenan was comparable with commercially available superdisintegrants. Faster dissolution of the accommodated drug was achieved with modified k-Carrageenan which was comparable with dissolution of the tablet formulation containing other superdisintegrants. The competent concentration of k-Carrageenan was found to be 5-15% as tablet disintegrant. Modified k-Carrageenan might be encouraging tablet disintegrant in fast dissolving formulations and can be worn in direct compression method.

Keywords: k-Carageenan. Epichlorhydrin. Aceclofenac. Crosslinking. Superdisintegrant

INTRODUCTION

Therapeutics that has extremely reduced aqueous solubility, the solubility rate is generally the rate limiting pace and therefore exhibits an influence on drug bioavailability [1]. Aceclofenac is non steroidal anti-inflammatory safe drug, which is used in the prevention and treatment of rheumatoid arthritis and osteoarthritis. Aceclofenac belongs to class II drug in biopharmaceutics (BCS) classification i.e. low solubility and high permeability [2].

The orally administered compressed tablet is the most extensively used solid unit dosage form for delivering therapeutics to patients. Additives play an essential role in the design of the tablet formulation by measuring its activity and ability [3]. Among the tablet additives or excipients, disintegrants are often treated as the most notable as they ensure the disintegration of the dosages form into smaller fragments upon administration, to allow the onset of pharmaceutical dissolution and consequent absorption [4,5].

The general objective of combining one or more disintegrants in the formulation is to enhance the surface area of the dosage form and soften the binding substance and associate together the solid granules that make up the final product. The total effects is that a tablet when disclosed to aqueous media disintegrates first into granules, and then into fine particles [6,7]. The rate of dissolution increases as the particle size reduces and is greatest when the tablets or capsules reduced to fine colloidal particles. Enhanced dissolution increases the rate of absorption of the drug, producing the desired pharmacological action. Various kinds of disintegrant have been identified and used since a long time [8].

Carrageenans are classified under hydrocolloids sourced from certain red seaweeds, the *Rhodophyceae* class algae that belong to the genera *Hypnea*, *Eucheuma*, *Gigartina*, *Chondrus* and *Lridaea* [9,10]. k-Carrageenan is specially procured from the extraction of the *Kappaphycus alvarezii* tropical seaweed, generally known as *Eucheuma cottonii.* Modification of k-Carrageenan caused swelling property which is an essential parameter for the disintegrant [11].

The purpose of the present investigation is to explore the feasibility of preparing a modified k-carrageenan and to evaluate its functionality as a superdisintegrants.

MATERIALS AND METHODS

Materials

Aceclofenac was procured from Ipca laboratories limited (Mumbai, India). k-Carrageenan was supplied by Mayor Corporation Pvt. Ltd. (Mumbai, India). Epichlorhydrin was procured from Spectrochem (Pvt. Ltd. (Mumbai, India). Croscarmellose Sodium (CCS) was purchased from Signet

Chemical Corporation Pvt. Ltd. (Mumbai, India). Crosspovidon (CP) was purchased from ISP Technologies Inc. (United States). Sodium starch glycolate (SSG) and Maiz starch (MS) were rocured from Sigma Chemical Co (St. Louis, MO). (Mumbai, India). Dibasic calcium phosphate anhydrous (DCPA), Klucel LF (L-HPC) and Magnesium stearate were supplied from Himedia (Mumbai, India). All other reagents and solvents used were of analytical or HPLC grade.

Methods

Synthesis and optimization of modified k-Carrageenan by chemical cross-linking

Modified k-Carrageenan was prepared by chemical cross linking method (Table I). Weighed quantity of k-Carrageenan (in varied ratio) was mixed in an alcoholic alkaline solution (KOH 700 mm and isopropyl alcohol 50% *v/v*). The cross-linking agent i.e. epichlorhydrin was added with stirring and left to react for different reaction time (varied in 1hr and 24 h) and at different temperature (RT to 50-60). After completion of reaction time the product was washed extensively with different solvents like ethanol, cold distilled water and hot (70-80°C) distilled water [12,13].

Prepared batches were optimized by swelling degree. In this test 500 mg of powder from each batch was kept in test tube containing distilled water. At the end of 24 h, swelling degree measured in term of increased in volume. To determine the overall swelling features, the swelling index test method is used [14].

To measure the sample swelling degree of pre-weighed dry samples were immersed in distilled water until maximum swelling was reached. After excessive surface water had been removed with filter paper, the weights of swollen samples were measured. The swelling index was determined by:

Swelling Index (SJ) = [{Wt – W0}/ W0)] x 100 Eq. (1)

Where, Wt = Mass of wet sample at time t

W0= Mass of dry sample at t=0

The swelling behaviours of all optimized formulations that resulted in peak swelling were further researched for swelling index measurement and contrasted with maize starch, crosspovidone (polyplasdone XL), croscarmellose sodium (Ac-Di-Sol), sodium starch glycolate (Primojel), unmodified k-Carrageenan and prepared modified k-Carrageenan swelling index (Table II).

Table I: Preparation of batches of modified k-Carrageenan with different reaction condition

Batch No.	Ratio of k-carrageenan *vs* epichlorhydrin (*w/w*)	Washed with cold water	Washed with hot water	Washed with ethanol	Temperature (°C)	Reaction time (h)
V1	0.6:1		✔		37±2	1
V2				✔		
V3			✔			24
V4				✔		
V5	1.5:1				37±2	24
V6						
V7	2:1		✔		37±2	1
V8				✔		
V9			✔			24
V10				✔		
V11	3:1	✔			37±2	1
V12			✔			
V13				✔		
V14		✔				24
V15			✔			
V16				✔		
V17	4:1		✔		37±2	1
V18				✔		
V19	6:1		✔		37±2	24
V20				✔		
V21		✔			55±2	24
V22			✔			
V23				✔		
V24		✔			37±2	1
V25			✔			
V26				✔		
V27	7:1		✔		37±2	24
V28				✔		
V29	13:1		✔		37±2	24
V30				✔		

Table II: Swelling index measurement and contrasted with maize starch, crosspovidone (polyplasdone XL), croscarmellose sodium (Ac-Di-Sol), sodium starch glycolate (Primojel), unmodified k-Carrageenan and prepared modified k-Carrageenan swelling indices

Material	Swelling index (%)
Maize starch	50±5
Crosspovidone (Polyplasdone XL)	1150±25
Croscarmellose sodium (Ac-Di-Sol)	1490±28
Sodium starch glycolate (Primojel)	1980±52
Unmodified k-Carrageenan	425±25
Modified k-Carrageenan	
V5	2055±48
V13	2120±52
V16	1240±34
V19	1559±43
V25	1288±35

Results are represented as mean ± SD (n = 3)

Evaluation of modified k-Carrageenan

Particle size distribution

The speed and force of disintegrating action may depend on the particle size of disintegrants. The size distribution profile of unmodified k-Carrageenan and modified k-Carrageenan was determined by employing Malvern Mastersizer (Mastersizer 2000 version 5.3, Malvern Instruments Ltd. UK) using dry method. Various formulations suitably diluted with distilled water were dropped into the Zetasizer electrophoretic cell for Zeta potential determination.

Aqueous solubility

Aqueous solubility has been carried out by the measurement of amount of distilled water needed to dissolve l gm of the sample. The solution was prepared by heating k-Carrageenan dispersion and modified k-Carrageenan separately in 80°C warm water bath.

Viscosity study

Increased cross linking density reduces polymer viscosity. Transfer 7.5 g of the dried sample to 600 ml of a beaker and spread in 450 ml of deionized water with agitation for 10 to 20 min. Add enough water to bring the final weight to 500 g and heat in a continuously agitated water bath until 80°C (20-30 min) temperature is reached. Add water in a constant temperature bath at 75°C to adjust for loss by evaporation, cool to room temperature (35±3°C).

The Brookfield viscometer was used to determine the flow properties of various formulations. Evaluation of the physical stability of systems was carried out by visual inspection of formulations and by performing the rheological measurements. The DVII+ Pro Brookfield Viscometer (Brookfield Engineering Laboratories, Stoughton, MA, United States, with software) with small sample adaptor (spindle and chamber SC4-18/13R) was used to determine flow properties of the various formulations between the percentage torque values of 10-100.

Gel strength study

Free-radical crosslinking synthetic superabsorbent copolymers and outcomes stated that superabsorbent polymers (SAPs) with elevated water absorption were accompanied by low gel strength and high calculated molecular weight value. The modified and unmodified Formulated k-Carrageenan was placed in the test tube and gelled at 80°C. The gel resistance measuring device (locally fabricated) was then put on the gel. The time taken by the device to pass through the prepared gel to a depth of 5cm for each formulation was evaluated.

IR spectroscopy study

In determining the degree of substitution, the FT-IR spectra of the modified and unmodified samples was recorded with a Bruker IR spectrophotometer (INVENIO**, USA)** between 400 and 4000 cm^{-1}. The samples have been evaluated as pellets of potassium bromide (KBr).

Trace analysis of epichlorhydrin

Toxicology studies indicate that epichlorhydrin has serious toxic impacts on humans [15], both acute and chronic. The main analytical method available for epichlorohydrin quantification in water includes gas extraction technique [16].

Standard epichlorhydrin solution was prepared by blending 100 mg of epichlorhydrin in 100 ml of ethanol (1000 PPM). Diluting 5 ml stock solution with 50 ml methylene oxide (100 PPM) was the standard solution. The separating funnel was closed and shaken forcefully to release surplus pressure for l-2 min with regular ventilation. After the funnel was still in for 10 ml and extract was gathered for organic layer. Using fresh parts of solvent, extraction was repeated twice. The resulting three extract parts were mixed and the solvent evaporated to near dryness. With 1 ml of methylene chloride, the residue was dissolved and moved to the sample vial for gas chromatography (7890A GC System, Agilent Technologies, US) analysis. Chromatographic conditions are given in Table III.

Table III: Gas chromatography conditions

Parameters	Specifications
Column	Agilent J & W DB-5ms Ultra inert, 10m*x 0.18mm, 0.36µm
Carrier gas	Helium, Constant flow mode, 1.5ml/min
Inlet	Pulsed split 24.6 psi at 250c split 5:1
Oven Temperature	30°C (1 min); 20°C/min to 100°C (2 min)
Detector	FID at 260°C
Detector gas	Helium 30ml/min, air 400 ml/min, makeup (nitrogen) 25ml/min
Injection size	4µL

Tablet formulation for comparative assessment of the disintegrating impact of modified k-Carrageenan

The aim of the present research was to assess superdisintegrant property of k-Carrageenan in tablet formulation. For comparative assessment of the disintegrating impact of altered k-Carrageenan, different formulations with anhydrous di-calcium phosphate as model water insoluble diluents and having the same concentration of different disintegrating agent were prepared.

Preparation of tablet by direct compression method using model drug: Aceclofenac

Tablets were prepared according to the formula provided in Table IV by direct compression technique using tablet punching machine (Rotary Tablet Machine, Karnavati, India). All components were individually and weighed by 60 mesh sieve. They were blended in geometric proportion and tablets were prepared by direct compression using 8.6 mm flat round punch sizes using manually operated tablet punching machine.

Table IV: Formula table for Comparative evaluation of disintegrating properties of modified k—Carrageenan in tablet formulation

Ingredients	Batch Code									
	DCPA-CCS	DCPA-CP	DCPA-SSG	DCPA-MS	DCPA-UKC	DCPA-MKC-V5	DCPA-MKC-V15	DCPA-MKC-V19	DCPA-MKC-V22	DCPA-MKC-V25
Aceclofenac :Class II drug (mg)	200	200	200	200	200	200	200	200	200	200
Crosscarmellose Sodium (Ac-Di-Sol)	5%	-	-	-	-	-	-	-	-	-
Crosspovidon (Polyplasdon XL)	-	5%	-	-	-	-	-	-	-	-
Sodium starch glycolate (Primojel)	-	-	5%	-	-	-	-	-	-	-
Maize starch	-	-	-	5%	-	-	-	-	-	-
Unmodified k-Carageenan	-	-	-	-	5%	-	-	-	-	-
Modified k-Carageenan	-	-	-	-	-	5%	5%	5%	5%	5%
Magnesium stearate	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%
Dibasic calcium phosphate anhydrous (DCPA)	q.s.*	q.s.*	q.s.*	q.s.*	q.s.*	q.s.*	q.s.*	q.s.*	q.s.*	q.s.*
Total (mg)	260	260	260	260	260	260	260	260	260	260

*Quantity Sufficient

Determination of effective concentration of modified k-carrageenan a disintegrating agent

Tablets with distinct concentrations of altered k-carrageenan (1-15%) were prepared using Diclofenac as a model drug to determine the efficient concentration of modified k-carrageenan as a disintegrating agent when used in direct compression (Table V).

Table V: Formula of batches prepared by using varied concentration of modified k-Carrageenan

Ingredients	MKC-1%	MKC-3%	MKC-15%
Aceclofenac: Class II drug (mg)	200	200	200
Modified k- Carageenan (%)	1	3	15
Magnesium stearate (%)	1	1	1
Dibasic calcium phosphate anhydrous (DCPA)	q.s.*	q.s.*	q.s.*
Total (mg)	260	260	260

*Quantity Sufficient

Post compression characterization of aceclofenac tablet formulation

Tablet Thickness

Micrometer was used for the measurement of thickness of tablet. Ten tablets were taken and their thickness recorded.

Hardness

Hardness or tablet crushing force implies the force needed to break a tablet in a diametric compression has been determined using the Monsanto tablet hardness tester (Labotech, India).

Friability

Roche friabilator (Panomex Inc, India) was used to determine the tablet's friability. This machine subjects the tablet to the combined impact of abrasion and shock in a 25 rpm rotating plastic chamber and dropping a tablet in each revolution at a height of 6 inches. Pre-weighted (W1) tablet sample was put in the friabilator and the 100 revolutions were subjected. Tablets were powdered and reweighed after testing (W2). The following formula gives the percentage friability (F):

$$F\ (\%) = W1 - W2/W1 \times 100 \qquad \text{Eq. (2)}$$

Where, W1 = Weight of tablets before testing

W2 = Weight of tablets after testing.

Disintegration time

The time of disintegration was evaluated using a disintegration device. The time has been registered for the tablet to totally disintegrate into small particles. Tablet in each tube was introduced with disc and the tube assembly was placed in the beaker containing the disintegration media. The disintegration medium used was phosphate buffer (pH 6.8). Time taken for the tablet to disintegrate into small particles was recorded. Disintegration tests for tablets from each batch were conducted in triplicate.

Swelling index of tablets

A piece of tissue paper folded twice was placed in a small petri dish containing 6 ml of water. A tablet was put on the tissue paper and allowed to completely swell. The swelled tablet was then weighed. Swelling index (SI) can be calculated by following formula:

$$\text{Swelling index (SI)} = \frac{Wa-Wb}{Wa} \times 100 \qquad \text{Eq. (3)}$$

Where,

Wa = Weight of tablet after swelling

Wb = Weight of tablet before swelling

***In-vitro* dissolution studies**

The tablets containing model drug (aceclofenac) were subjected to *in-vitro* dissolution test using the following mentioned technique. The dissolution studies were carried out using USP type II devices, rotated at 75 rpm. The dissolution medium used was 900 ml of phosphate buffer (pH 6.8). The dissolution medium temperature was maintained at 37±0.5°C. At a particular time interval, i.e. 10, 20, 30, 40, 50, 60 minutes aliquot of the dissolution medium was removed and filtered. The dissolution medium was replaced with same amount of fresh phosphate buffer (pH 6.8) solution to maintain the sink condition. UV spectroscopy (UV visible spectrophotometer, Shimadzu-1800, Japan) verified the absorption of the filtered solution for aceclofenac at λmax 273.5nm and determined the drug content from the standard calibration curve.

Statistical analysis

Statistical data analysis was done using computer package SPSS version 16 (Chicago, IL). Data are presented as the mean standard deviation (SD).

RESULTS AND DISCUSSION

Synthesis of modified k-Carrageenan as disintegrant to enhance the solubility

In chemical crosslinking of k-Carrageenan, the maximum swelling graph was observed in Formula V19 where the ratio of k-Carrageenan was 6:1, the reaction time was 24 hours, and hot water (70-80°C) was used as a solvent for the final product washing. Moderate to significant swelling also observed in formula V5, V15, V22 and V25.

Characterization of modified k-Carrageenan

Particle size analysis

Prepared modified k-Carrageenan evaluated for particle size distribution (PSD). PSD of modified k-Carrageenan was compared with PSD results of the unmodified k-Carrageenan. It can be seen from Fig. 1 and Fig. 2, the particles of unmodified k-Carrageenan were of narrow range while particles of modified k-Carrageenan were of wide range, which showing modification has been carried out. Larger particle exert more swelling pressure than smaller one as they swell to larger extent which can result in rapid disintegration.

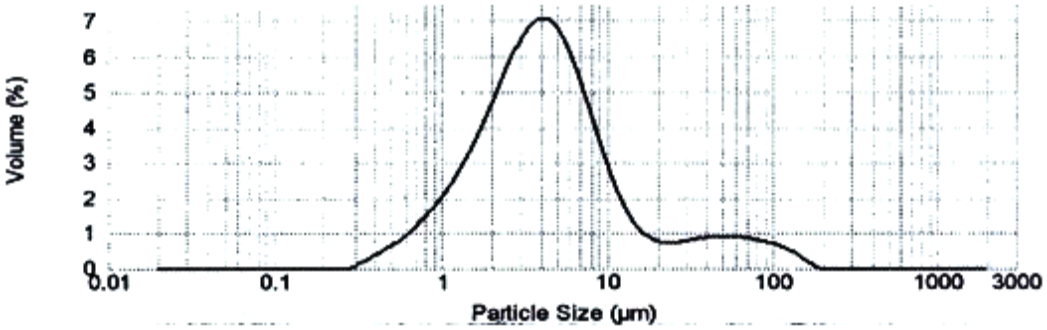

Figure 1: Particle size distribution (PSD) Plot for unmodified k-Carrageenan

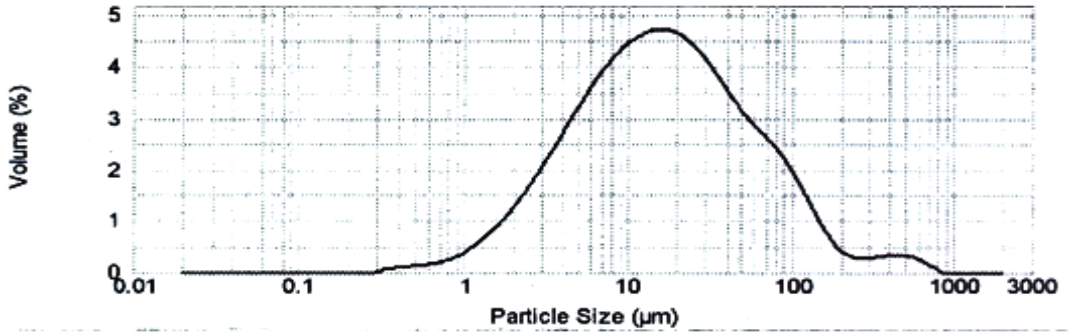

Figure 2: Particle size distribution (PSD) Plot for modified k-Carrageenan

Solubility study

It can be seen from Table VI that 27 ml water required for the 1 gm of unmodified k-Carrageenan while 39 ml required for solubilizing 1 gm of modified k-Carrageenan indicating solubility of modified form of k-Carrageenan has been reduced due to increased molecular weight because of crosslinking. When a polymer is crosslinked, the entire polymer average molecular weight is boosted, leading in lower solubility. This can therefore be considered as an indication of crosslinking.

Table VI: Results of solubility study

Polymer	Solubility
Unmodified k-Carrageenan	27 ml for 1 g
Modified k-Carrageenan	39 ml for 1 g

Results are represented as mean ± SD (*n* = 3)

Viscosity determination

It can be seen from Table VII that viscosity of unmodified k-Carrageenan was 50.5 CPS while viscosity of modified k-Carrageenan was 48.6 CPS indicating viscosity of modified form of k-carrageenan reduced as crosslinking density decreases viscosity of polymer.

Table VII: Results of viscosity study

Polymer	Concentration % (*w/v*)	Temperature (°C)	Viscosity (CPS)
Unmodified k- Carrageenan	1.5	35±3	50.5±5
Modified k-Carrageenan	1.5	35±3	48.6±4

Results are represented as mean ± SD (*n* = 3)

Gel strength Study

It can be seen from Table VIII unmodified k-Carrageenan formed strong gel while modified k-Carrageenan formed weaker gel indicating modified form of k-Carrageenan had crosslinked accompanied by low gel strength.

Table VIII: Results of gel strength study

Polymer	Gel strength (Sec)
Unmodified k-Carrageenan	65±5
Modified k-Carrageenan	25±2

Results are represented as mean ± SD (*n* = 3)

IR spectroscopy study

k-Carrageenan has absorption bands, typical of all polysaccharides, in the 1000 to 1100 cm^{-1} region. Characteristic absorption bands (Figs. 3 and 4) and intensities are given in Table IX.

Unmodified k-Carrageenan shows peaks at 1234.48 cm^{-1}, 923.93 cm^{-1} and 846.78 cm^{-1} indicating ester sulphate, 3, 6-anhydrogalactose, Galactose-4-sulphate group respectively. In addition it also shows peak at 1004.95 cm^{-1} and l068.6 cm^{-1} which can be due to C-H stretching. The IR of modified k-Carrageenan is different from unmodified k-Carrageenan indicating formation of a new product. Reaction of epichlorhydrin with polysaccharide having galactose group generally results in etherification of free hydroxyl group which is indicated by intense peak near 1150 cm^{-1} in modified k-Carrageenan.

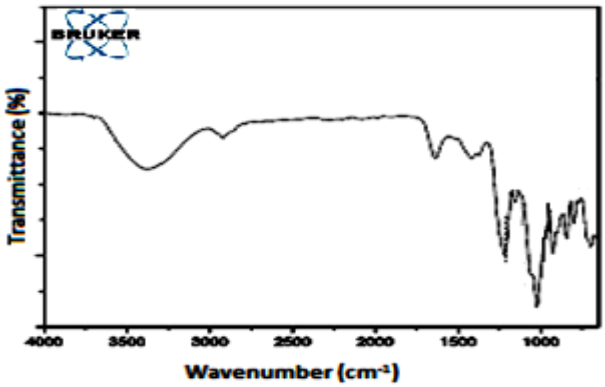

Figure 3: FT-IR Spectrum of unmodified k-Carrageenan. FT-IR spectral analysis shows the characteristic absorption bands of polysaccharides in the region of 1000 to 1100 cm^{-1}.

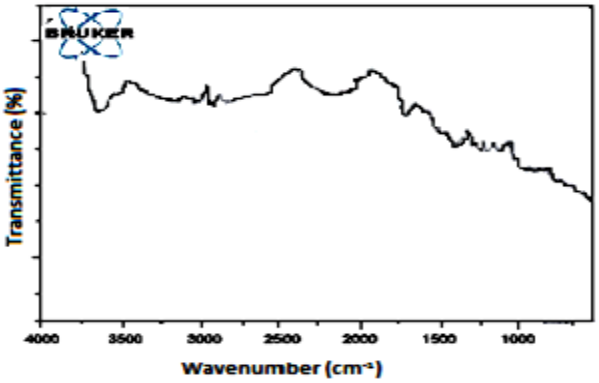

Figure 4: FT-IR Spectrum of modified k-Carrageenan. FT-IR spectral analysis shows the characteristic absorption bands of etherification of free hydroxyl group due to reaction with epichlorhydrin near 1150 cm^{-1} in modified k-Carrageenan

Table IX: Characteristic absorption bands of unmodified k-carrageenan and modified k-Carrageenan

Characteristic absorption bands		Unmodified k-carrageenan		Modified k-carrageenan	
Wave number (cm^{-1})	**Molecular assignment**	**Peak**	**Intensity**	**Peak**	**Intensity**
1220-1260	Ester sulphate	1234.48	53.57	1203.62	61.903
				1255.70	61.902
918-933	3,6-anhydrogalactose	923.93	52.30	931.65	59.92
840-850	Galactose-4-sulphate	846.78	53.44	840.90	59.54
1000-1100	C-O-C stretch	1157.33	55.85	1145.75	59.54

Trace analysis of linker

Chromatograph of sample (modified k–Carrageenan, Batch code: V19) is not showing any peak for epichlorhydrin (Fig. 7) indicating absence of free epichlorhydrin in the product, while comparing with the chromatographs of blank and standard chromatographic solutions (Figs 5 and 6).

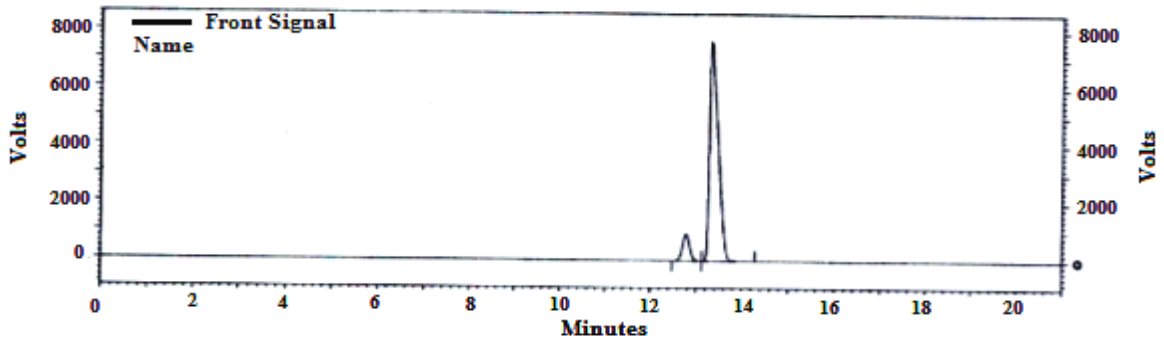

Figure 5: GC Chromatogram of blank solution of dichloromethane (DCM) with Methanol

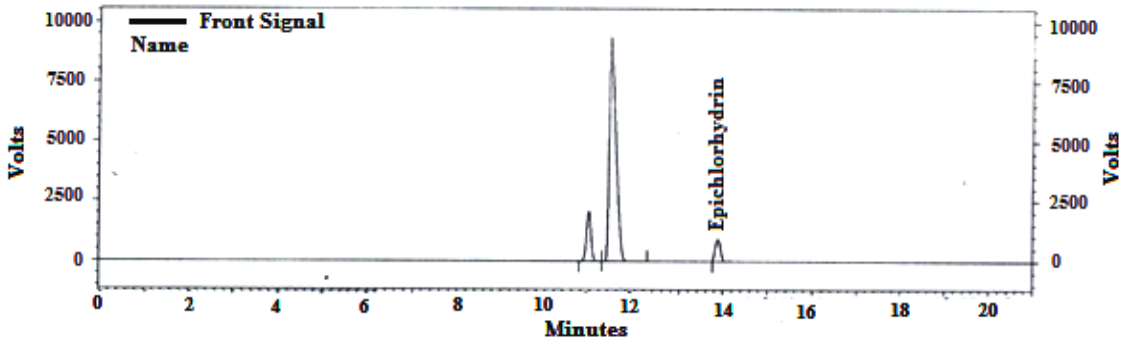

Figure 6: GC Chromatogram of standard solution of epichlorhydrin (crosslinking agent) along with dichloromethane (DCM) and methanol

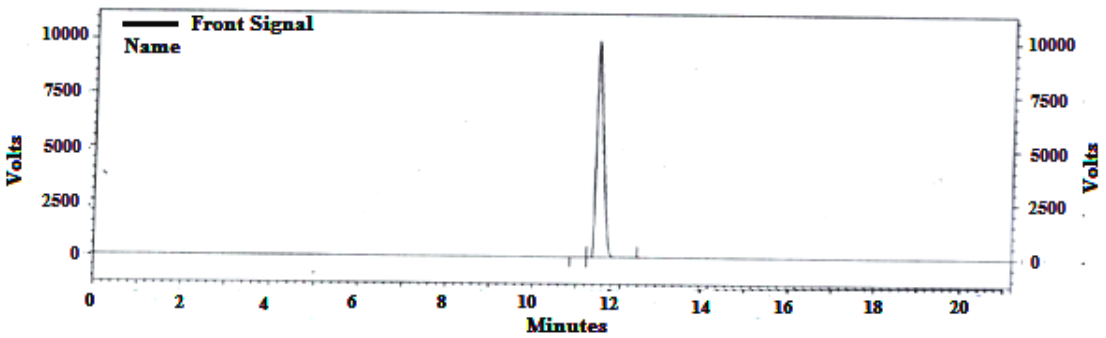

Figure 7: GC Chromatogram of sample: modified k-Carrageenan (Batch V19) along with dichloromethane (DCM)

Post -compression evaluation of aceclofenac tablet

Formula DCPA-CCS, DCPA-CP, DCPA-SSG tablets were prepared using superdisintegrant and DCPA-MS and DCPA-UKC prepared using starch and unmodified k-Carrageenan and formula tablets DCPA-MKC-V5, DCPA-MKC-V15, DCPA-MKC-V19, DCPA-MKC-V22, DCPA-MKC-V25 were prepared using modified k-Carrageenan of various batches as disintegrant.

It can be seen from Table X that disintegration time of tablets prepared using modified k-Carrageenan was comparable with the tablets prepared using superdisintegrants [17,18]. Swelling index of tablets of the formulation DCPA-MKC-V19 where modified k-Carrageenan (V19) was used as disintegrant was comparable with the tablets prepared using superdisintegrants.

Results of studies have shown (Table X) that with increasing hardness, disintegration also improves in all formulas prepared with superdisintegrants or altered k-Carrageenan as a disintegrant [19].

Percentage (%) cumulative drug release studies have been performed for the following batches i.e. DCPA-CCS, DCPA-CP, DCPA-SSG, DCPA-MS, DCPA-UKC, DCPA-MKC formulation prepared by direct compression in which aceclofenac (class II drug) as a model drug and 5% disintegrant concentration used. It can be seen from table XI that at the end of 30min, formulation DCPA-CCS, DCPA-CP, DCPA-SSG containing superdisintegrants (CCS, CP, SSG) shows 55.6%, 76.6%, 90.25% cumulative drug release. DCPA-MS containing traditional disintegrant (Starch) shows 27.75 % cumulative drug release (% CDR). DCPA-UKC, DCPA-MKC prepared using unmodified k-Carrageenan and modified k-Carrageenan as disintegrant respectively showing 28.87% and 92.81% CDR. It can be seen that % CDR of formulation with modified k-Carrageenan was much higher than formulation with traditional disintegrant and it was comparable with % CDR of formulation with SSG (Superdisintegrant) [20,21].

Table X: Result of post compression evaluation

Batch Code	Tablet Thickness (mm)	Tablet Hardness (Kg)	Friability (%)	Disintegration Time (S)	Swelling Index (%)
DCPA-CCS	3.5±0.14	3.4±1.0	0.056±0.03	12±1.0	182±08
DCPA-CP	3.5±0.12	3.2±1.1	0.040±0.02	11±1.0	144±05
DCPA-SSG	3.4±0.15	3.6±1.1	0.038±0.02	14±1.2	258±15
DCPA-MS	3.5±0.12	3.8±1.2	0.024±0.01	24±1.2	135±06
DCPA-UKC	3.4±0.14	3.9±1.2	0.054±0.02	64±2.2	105±05
DCPA-MKC-V5	3.5±0.12	3.2±1.4	0.040±0.02	11±1.0	185±08
DCPA-MKC-V15	3.5±0.13	3.2±1.5	0.061±0.04	12±1.1	260±10
DCPA-MKC-V19	3.4±0.11	3.8±1.5	0.059±0.03	15±1.0	125±04
DCPA-MKC-V22	3.5±0.14	3.2±1.1	0.052±0.02	12±1.0	166±06
DCPA-MKC-V25	3.5±0.14	3.1±1.2	0.035±0.01	12±1.2	145±05

Results are represented as mean ± SD (n = 3)

Table XI: Cumulative drug release (%) of formulation prepared using aceclofenac (class-II) by direct compression

Time (min)	Cumulative Drug Release (%)					
	DCPA-CCS	DCPA-CP	DCPA-SSG	DCPA-MS	DCPA-UKC	DCPA-MKC
10	44.80±2.2	50.40±2.8	23.06±1.8	10.12±1.2	10.31±2.0	65.62±4.2
20	47.40±2.4	63.50±4.1	75.37±4.9	22.68±2.1	28.12±2.5	88.50±6.8
30	55.60±4.2	76.60±4.5	90.25±6.1	27.75±2.2	28.87±2.4	92.81±8.8
40	70.10±6.1	80.40±5.2	92.12±6.5	33.93±2.4	32.62±3.2	96.00±8.4
50	75.90±6.5	81.90±5.8	94.06±6.6	36.18±3.1	36.93±3.6	96.75±8.4
60	90.50±6.8	95.00±6.1	96.00±6.2	46.68±4.8	48.56±4.8	97.31±8.9

Results are represented as mean ± SD (n = 3)

CONCLUSIONS

Fast disintegration of tablet is a criterion for ensuring unrestricted conduct in drug dissolution and drug accessibility for bioavailability. Faster drenching of a disintegrating system chaperone by fast protuberance is contemplated as the most coherent necessity for super disintegration. Manipulation in natural polysaccharide are often accomplished to have desired characteristics such as prompt wetting and rapid swelling without the forming of viscous gel that could obstruct dissolution [22]. A small effort was made in the present research to modify k-Carrageenan (marine polysaccharide) by using epichlorhydrin as a crosslinker. Modified k-Carrageenan was analyzed for swelling index, PSD, solubility, viscosity, gel strength, and FT-IR after optimizing the system. Modified k-Carrageenan exhibited an index of swelling similar to superdisintegrants such as croscarmellose sodium (CCS), crosspovidone (CP), sodium starch glycolate (SSG) and starch (traditional disintegrant) and contrasted for its disintegrating impact using aceclofenac (BCS Class II) as model drug.

The time of disintegration of tablets prepared with altered k-Carrageenan as a disintegrant was similar to that prepared with superdisintegrants. Modified k-Carrageenan as a disintegrant in a tablet formulation resulted in comparatively rapid and higher dissolution of 92.8 percent for cumulative drug release (CDR) of the contained drug at the end of 30 min, which was comparable to the dissolution of superdisintegrant formula.

Thus, it can be concluded that using epichlorhydrin as a crosslinking agent, k-Carrageenan, a marine polysaccharide can be altered by chemical technique. Modified k-Carrageenan can be adapted as a disintegrant as it demonstrates the action of disintegration and its impact on the *in-vitro* dissolution of BCS Class II drug (aceclofenac). The altered k-Carrageenan in tablet formulations has been invented to be a promising superdisintegrant and can be used as an efficient disintegrant in the formulation of fast dissolving tablets in a concentration of 5-15 percent.

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Conflicts of Interest

The authors declare no conflict of interest

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