FORMULATION AND EVALUATION OF OFLOXACIN POLYHERBAL TOPICAL GEL

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ABSTRACT

Ofloxacin is a synthetic fluorquinolone (fluoroquinolones) antibacterial agent that inhibits the super-coilingactivity of bacterial DNA gyrase, halting DNA replication. Topical gel formulations of Ofloxacin were developedby using gel forming agent like Carbopol 934P. Chitosan, Neem, a n d Turmeric were used as woundhealing modifiers in different concentrations. Glycerin was used as humectants. The gel formulations werecharacterized by IR study suggested that the formulations prepared are a physical mixture. The prepared gelformulations were evaluated for drug content, pH and rheological parameters like viscosity, spreadability andextrudability. The prepared gels were also evaluated for in-vitro diffusion study. The percent release ofOfloxacin from plain gel containing alone Ofloxacin was slow as compared to other gel formulations containingdifferent wound healing modifiers. The formulation (F2) containing 1% Ofloxacin along with 2% chitosan showedmaximum percent release . The gels were also evaluated for in vivo wound healing activity. All the gelformulations showed more than reduction in wound. The gel formulation (F6) containing Ofloxacin alongwith 1% chitosan and 1% turmeric showed 99.1% reduction in wound area after 12thday. Hence, from the overallstudy it was concluded that Ofloxacin gels along with wound healing modifiers would be promising in the effectivemanagement of wounds.

Keywords: Ofloxacin, Turmeric, Neem, Chitosan, Aloevera, Carbopol 934P

INTRODUCTION

Gel is a semi solid formulation that has a pair of components which is liquid phase in rich. It have a character the continuous structure show like slid properties. After the application of gel the liquids are drying by the evaporation and, gels of drug are covering the skin [1].

Gels are as compare to the creams and other ointments give better drug release. These are highly bio-compatible that's why minimum risk of adverse reaction and inflammation. The dermatological use of gels have many property as thixotropic, easily remove, non- greasy, desirable spreadable, non-staining, emollients, compatible with the many excipients. Topical drug delivery systems are apply as directly on the body surface as external part by spraying, rubbing, spreading. The topical rout of administration are very common and it is use as treatment of skin disorder and local effects.[2] Gels are often topically applied as emollients , or as occlusive dressing and also as protective for the local and systemic

medication. Gels are defined as significant extent dilute cross linked system that is in the steady state no flow. Gels are sometimes called jellies.

The word gel was invented by 19thcentury by Scottish chemist Thomas graham by the clipping from gelatin.

Gels are semisolid systems that are a polar phase is constrained within a three dimensional polymeric matrix in which high degree of physical and sometimes chemical cross linking has been introduced. The polymers apply in the preparation of pharmaceutical gels including natural gum semi synthetic and synthetic materials. Natural gums as tragacanth, pectin, agar, alginic acid, carrageen and such semisynthetic materials as carbopols, sodium alginate, methyl cellulose, carboxymethyl cellulose, hydroxyethyl cellulose, where is synthetic polymer such as vinylpolymers with ionizable carboxyl groups. Gels are prepared by mainly fusion process by the gelling characters of gallant

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DRUG PROFILE

Structure:

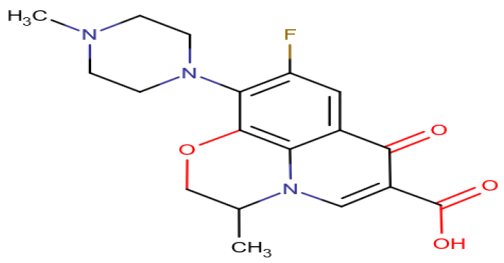

Figure no. 1: Structure of ofloxacine

I.U.P.A.C. Name:
7-fluoro-2-methyl-6-(4-methylpiperazin-1-yl)-10-oxo-4-oxa-1-azatricyclo[7.3.1.0^{5},^{13}]trideca-5(13),6,8,11-tetraene-11-carboxylic acid.

Table No.1: PHYSIOLOGICAL PROPERTIES

Appearance	A odorless yellow crystalline powder		
Solubility	The solubility of ofloxacine in various solvent system at room temprature (25^{O}c)is below, in the term of current USP system		
	S.N.	SOLVENT	SOLUBILITY

	1 2 3 4 5 6 7 8 9	Methanol DCM Ethanol Acetone Choloroform Ether HCL N-octonol Water	springly solube freely soluble freely soluble springly soluble slightly soluble insoluble soluble soluble freely soluble
Chemical formula	$C_{18}H_{20}FN_3O_4$		
Description	This compound belongs to the class of organic compounds known as Quinoline carboxylic acids. These drug type of Quinolones in which the Quinoline ring system is substituted by a carboxyl group at one or more positions		
Molecular weight	361.373 g/mole.		
Dose	200-400 mg tab , 20mg IV, 0.3% opthalmic		
Melting Point	254^{o}C		
Metabolism	Hepatic metabolism.		
Route of administration	Oral administration, Topical administration, Ophthalmic administration , Intra Venous administration.		
Side effects	Palpitation, postural hypotension, Reflex tachycardia, Edema, flushing, Fatigue, Dizziness, Sedation		
Pharmacodynamic	Ofloxacin is a quinolone/fluoroquinolone antibiotic. Ofloxacin is bactericidal and its mode of action depends on blocking of bacterial DNA replication by binding itself to an enzyme called DNA gyrase, which allows the untwisting required to replicate one DNA double helix into two. Notably the drug has 100 times higher affinity for bacterial DNA gyrase than for mammalian. Ofloxacin is an antibiotic which are comes under the classification of floroquinolone that is worldwide utilization against bacteria and bacterial disease. It is more active against both Gram-positive also against the negative bacteria.		

Mechanism of Action	Ofloxacin acts on DNA gyrase and toposiomerase IV, enzymes which, like human topoisomerase, prevents the excessive supercoiling of DNA during replication or transcription. By inhibiting their function, the drug thereby inhibits normal cell division.
PHARMACOKINETIC	
Absorption	Completely absorbed
Bioavailability	98%
Protein binding	32%
Half life	6 hours
Affected organism	Antibiotic (Fluoroquinolones)
Intraction	It intract with Sucralfate, or Iron suppliment, aceclofenac, acetylsalisalic acid, And some antacids drug, Didanosine may decrease effectiveness of this folroquinolones drug.
Food interaction Affected organism	Avoid high dose of caffeine. Take meals without regard. Enteric bacteria and other eubacteria.
Log p	0.79
Excretion	Renal
Elimination half life	11hours
Toxicity	LD_{50}= 5450mg/kg
State	Solid
Dissociation constant(pka)	6.2
Indication	It is effective against gram positive and gram negative bacteria including-psuedomonas gonorrhoea, E.coli, staphylococci, H. influenzza. Mainly used for GIT infection.
Contra indication	Children below 12^{th} year, convulsion pregnancy

	Lactation and hypersensitivity
Precautions	Spinal cord disease. Epilapcy , arterisclerosis in the brain.

MATERIALS AND METHODS

Materials:
Chitosan was obtained as gift sample from India Sea Foods, Cochin, Kerala and Ofloxacin was obtained as giftsample from Macleods Pharmaceuticals Ltd, Mumbai. Turmeric and Neem oil was obtained from the Jajee Stores,Gulbarga. Aloe vera was obtained from the Rajesh chemicals, Mumbai. Carbopol 934 was obtained fromLobachem Pvt Ltd, Mumbai. All other chemical used were of analytical grade.
Method:

Formulation of Ofloxacin gels
Different gel formulations were prepared containing 1%w/w of Ofloxacin using Carbopol 934P as gel baseaccording to the formula mentioned in the table 2 .

Procedure:
The gels were prepared by soaking 1% carbopol in 25ml of water for 24hrs and then neutralized with sufficientamount of triethanolamine, mixed well with glass rod and kept for 15 minutes. The drug was dissolved insufficient quantity of methanol. Accurately weighed quantity of turmeric (2%) was dissolved in sufficientquantity of distilled water and then added to the neutralized carbopol with continuous stirring. Finally the drugsolution was added to the neutralized carbopol solution with continuous stirring for about 30 mins to get a
sparkling clear gel. Finally the volume wa s made up to 50ml with distilled water with continuous stirring. The stirring was stopped periodically to expel the air entrapped during the process of stirring. Same procedure was followed for other remaining formulations containing different wound healing modifiers like chitosan, aloevera and neem

Table no. 2 list of formulation.

Ingredients	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**
Drug(Ofloxacin)	2	2	2	2	2	2
Sodium alginate	2	2	2	2	2	2
Chitosan	-	2	2	2	-	2
Neem	-	-	2	-	2	1
Turmeric	-	-	-	2	1	2
Ethanol	2.5	2.5	2.5	2.5	2.5	2.5

Glycerine	2.5	2.5	2.5	2.5	2.5	2.5
Triethanolamine	Q.S	Q.S.	Q.S.	Q.S.	Q.S	Q.S.
Methyl paraben	0.048	0.048	0.048	0.048	0.048	0.048
Propyl paraben	0.08	0.08	0.08	0.08	0.08	0.08
Water	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.

EVALUATION OF OFLOXACIN GEL FOR WOUND HEALING ACTIVITY

1. Measurement of pH

The pH of gel formulation was determined by digital pH meter. 1gm of prepared gel was dissolved in 10ml of distilled water then stay for 2 hours. This was followed for all formulation for pH determination. Each formulation was done by triplet. At last the value was calculated.

2. **Drug content analysis**

5gm of gel contain 100mg of drug was taken and transfer in to 100ml volumetric flask and volume made up with 7.4pH buffer. Sonicated for 30minutes and filtered further diluted it and absorbance was determined at 287nm by UV-Spectrophotometer. At last drug content was calculated.

3. **Viscosity study**

Viscosity of this prepared formulation was determined by the using of rotational viscometer (fungi lab) with the spindle no. PA, PC, PB, PD, PE, PF, and range of viscosity from 2-15rpm, at the individual rpm is higher torque was noted down and the mean calculated.

4. Spreadability

The evaluation of Spreadability of Ofloxacin gel was detected by measured the diameter 2gm of gel placed between the plates for 3 minutes. Gel made a uniform layer between plate by the spreading, then after weighed the upper plate tie gel and calculated that by using of bellowing formula.

$S=M\times L/T$

S= Spreadability (gcm^{-1}/sec)

M=weight of tied gel on the upper plate

L=length of glass slide

T=Time

5. Extrudability study

The prepared formulation of gel was filled in the collapsible tube then after gel stable in the container. The Extrudability was determine by the extruded the gel from tube. 1cm gel extruded out in 30sec.

6. In-vitro release study

In-vitro drug release study of the prepared Ofloxacin gel formulation was carried study by the diffusion cell.

Procedure: The diffusion release study of the gel formulation was carried out using by chambered of donor and receiver compartment model by the using of cellophane membrane or egg membrane. 5gm of

gel sample was hold on the membrane and fixed and one end of glass tube and it was dispersed on the phosphate buffer pH 7.4 buffer as dissolution medium. Then the every sample was withdrawn at a constant interval time of 1, 2, 3, 4, 5, & 6, hours.

PREPARATION OF CALIBRATION CURVE OF OFLOXACIN IN DIFFERENT SOLVENT SYSTEM

a. Preparation of calibration curve of Ofloxacin in 7.4 pH buffer

Table no. 3: Construction of Calibration curve of Ofloxacin in7.4 pH Phosphate buffer

S.No.	Concentration (µg/ml)	Absorbance(λ_{max} 287nm)
1	1	0.149
2	2	0.238
3	4	0.426
4	6	0.697
5	8	0.876
6	10	1.088

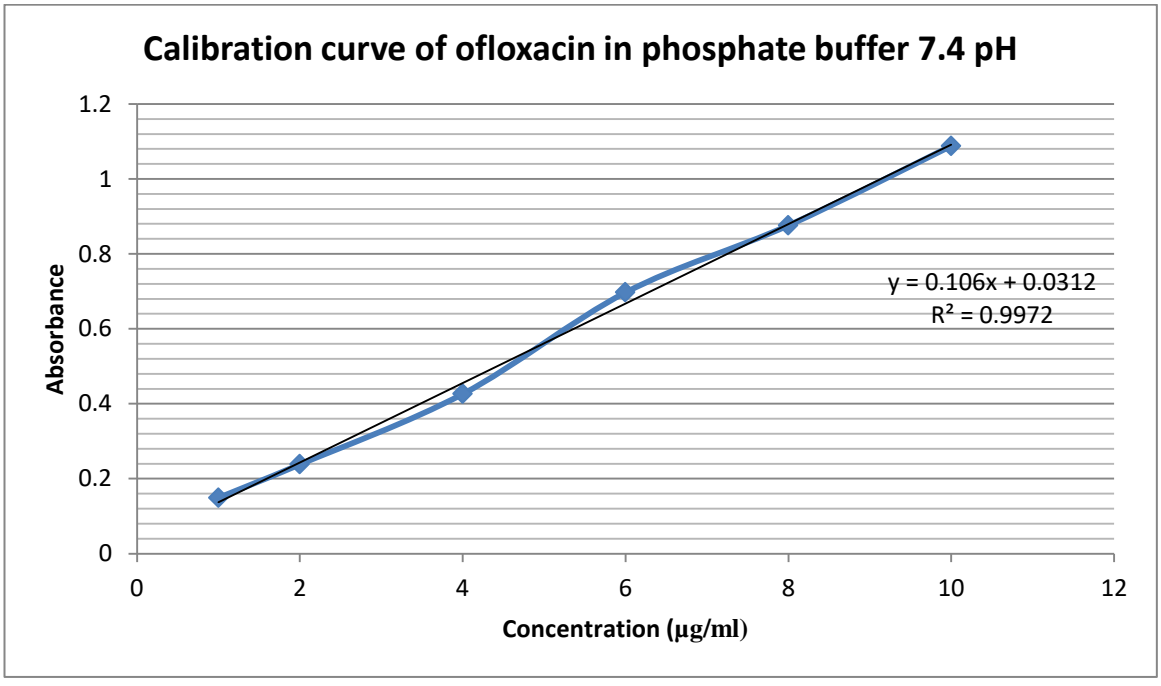

Fig no. 2: calibration curve of Ofloxacin in phosphate buffer

b. Preparation of calibration curve of Ofloxacin in water

Table No 4 : Construction of Calibration curve of Ofloxacin in water

S.No.	Concentration (µg/ml)	Absorbance(λ_{max} 287nm)
1	1	0.059
2	2	0.092
3	4	0.232
4	6	0.341
5	8	0.421
6	10	0.573

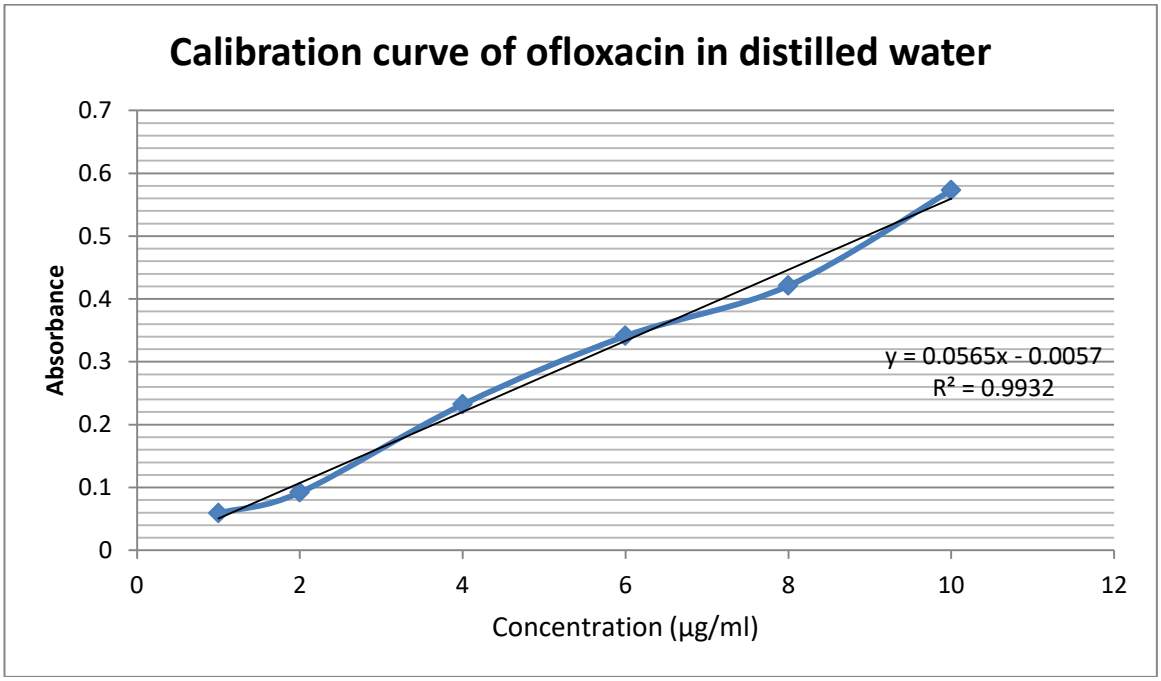

Figure no. 3 : calibration curve of Ofloxacin in distilled water

DRUG EXCIPIENTS COMPTABILITY STUDY

The drug of Ofloxacin and other excipients were taken in ratio 1:1 and well mixed that by using of poly bags. Then after mixture of drug and excipients was transferred from poly bag to glass vials & sample was put in to the stability chamber at 40 C for 21days

Through Fourier transform Infrared Spectroscopy: The compatibility study of drug excipients was done by FTIR analysis.

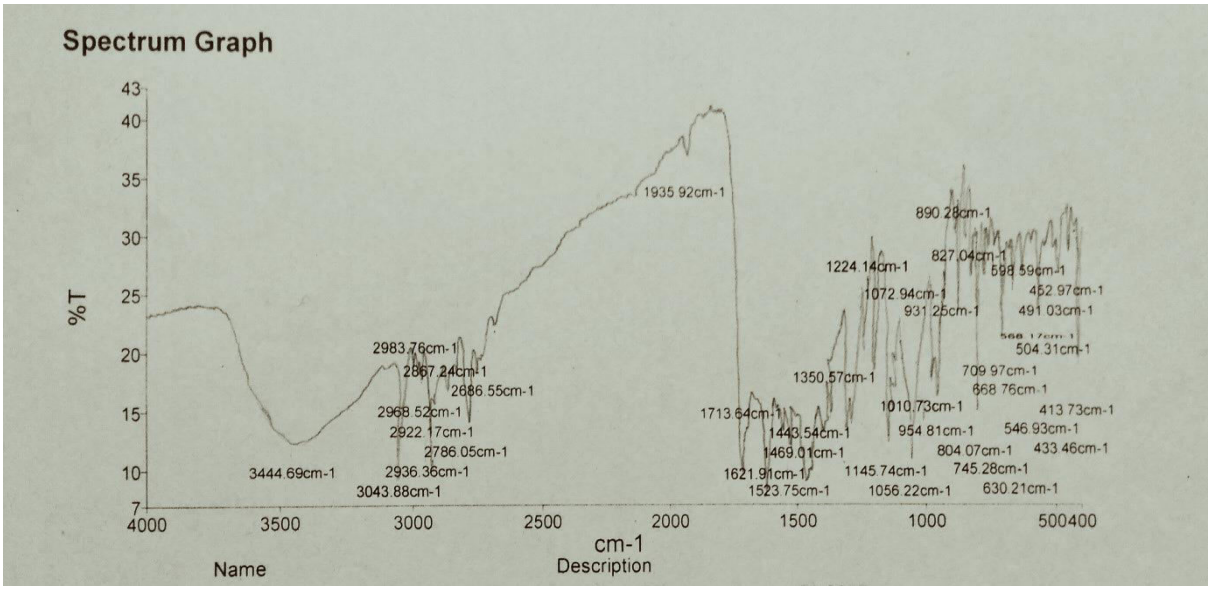

Figure no. 4 : FTIR spectra of pure drug Ofloxacin

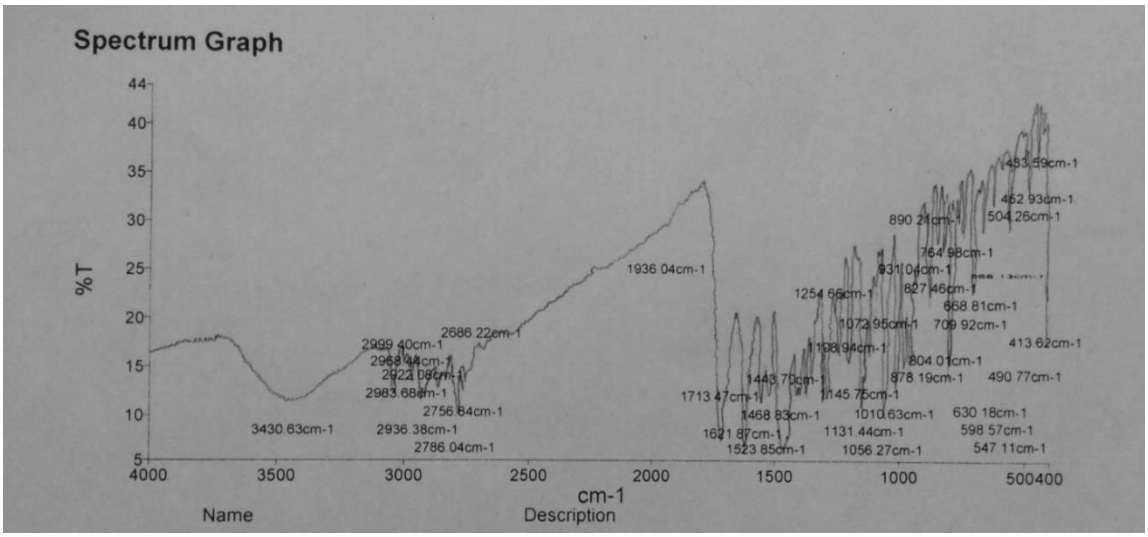

Figure no.5: FTIR spectra of pure drug and sodium alginate

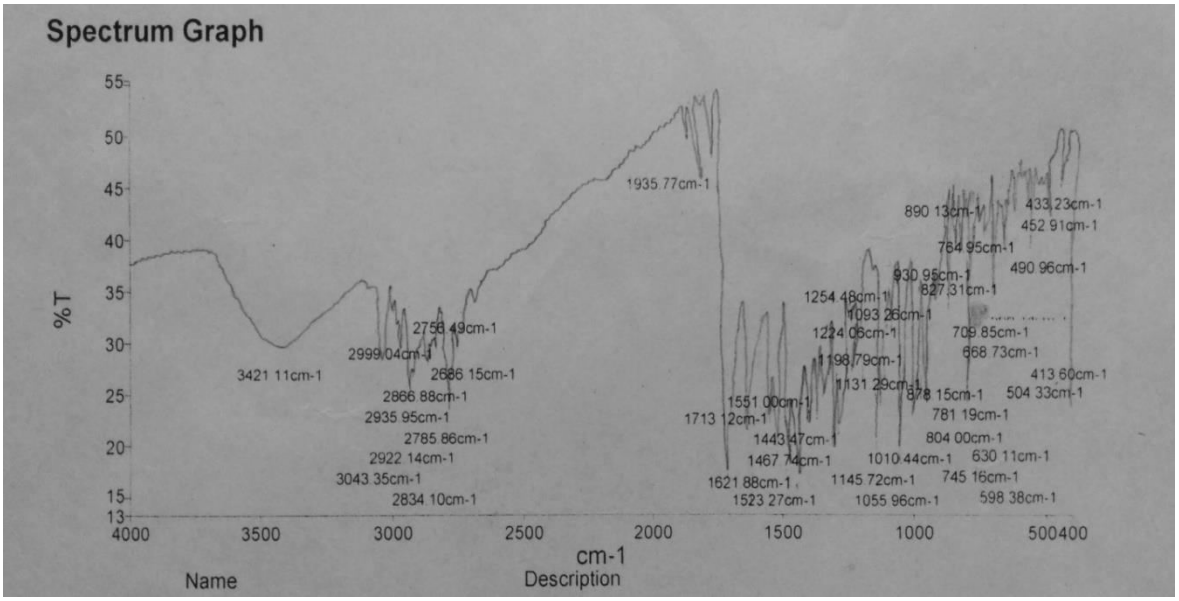

Figure no. 6 : FTIR spectra of drug and chitosan

CONCLUSION

The current designed formulation of gel was developed for the enhanced of pharmacokinetics behavior. In this formulation used turmeric and Neem for wound healing. Ofloxacin drug is an antibiotic and with combination of turmeric produced synergistic effects. The gel was prepared by the soaking method. Sodium alginate and chitosan was used in this. Chitosan have also wound healing property. There was developed 6 formulations and the 2 formulations was give best results. F3 & F6 was showing the better results as F3 (49.85%), F6 (49.44%) drug release at half- life of its, drug content (F3- 98.36%, F6- 97.31%), Antimicrobial effects, viscosity, Spreadibility was observed good.

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