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Formulation And Evaluation of Chlorhexidine, Aloe Vera Gel Sodium Alginate Beads Incorporated Gel for Topical Application

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Abstract

The aim of this project was to develop a novel gel formulation by incorporating chlorhexidine, aloe vera, and sodium alginate beads, and to evaluate its properties for potential pharmaceutical and therapeutic applications. The gel was formulated using aloe vera gel as the base, incorporating chlorhexidine as the antimicrobial agent, and sodium alginate beads for sustained release. The formulation process involved optimizing the concentrations of each component to achieve desired viscosity, drug release profile, and stability. Various physicochemical properties of the gel were evaluated, including pH, viscosity, drug content, stability, spreadability and rheological behavior. The developed gel exhibited desirable properties such as suitable pH, viscosity for topical application, controlled release of chlorhexidine, and significant antimicrobial activity against tested microorganisms. Stability studies indicated good shelf-life under recommended storage conditions. In conclusion, the formulated chlorhexidine-aloe vera-sodium alginate beads incorporated gel holds promise as a potential topical antimicrobial agent with sustained release properties, suitable for various pharmaceutical and therapeutic applications. Further studies including in vivo evaluations are warranted to validate its clinical efficacy and safety.

Keywords

Aloe vera Gel, Chlorhexidine, Alginate beads, Ionotropic Gelation, Entrapment Efficiency, *In-vitro* drug diffusion studies.

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INTRODUCTION:

Aloe vera (syn. Aloe barbadensis, Fam. Liliaceae), is also known as Aloe Barbados or Aloe Curacao, was being used in traditional and old medicines for several years for treatment and cure of variety of diseases. Aloe vera gel is proved to be safe when applied topically and shows only some allergic reactions being reported. The efficacy of aloe vera gel to treat burns, deep wounds, genital herpes, and dermatitis have reported in clinical trials, but other diseases such as psoriasis or internal usage for the treatment of type 2 diabetes is not fully known. The major use of aloe vera gel is as a skin moisturizer in cosmetic products and in treatment for sunburns, which it has proven it as effective.[1] Sodium alginate beads as the name indicates they are nearly spherical, small with diameter of 0.5-1000 micrometre in size, solid particles, free flowing carriers containing entrapped drug particles either in solution or crystalline form to facilitate a sustained release or multiple release profiles for treatment with various active ingredients avoiding major side effects. The alginate beads can be prepared from various polymers such as cationic polymers such as chitosan, anionic polymers such as sodium alginate, binding components such as gelatin, avidin,

chondroitin sulphate in required ratio and employing various methods such as Ionotropic gelation, Emulsification gelation etc. Aloe vera gel and Chlorhexidine incorporated alginate beads were prepared for topical application. Chlorhexidine shows antiseptic and Germicidal action and Aloe vera present along with the drug minimises the side effects of Chlorhexidine such as Skin irritation, rashes, Itching and provides emollient and soothing effect and enhances the solubility and penetration of drug due to its hydrophilic nature. [2] The alginate beads prepared are in turn incorporated into Gel formulation to convert it into a proper dosage form. Gels are desirable for topical application as it shows greater spreadability and faster penetration through the skin due to their lighter texture and hydrophilic and lipophilic properties. This helps in rapid wound healing and effectiveness.[3]. Further Evaluation studies were conducted on the formulations and reported.

MATERIALS AND METHODS:

Materials:

Chlorhexidine was obtained as gift sample from Pharmatrain, Hyderabad. Sodium alginate, HPMC K-15M, Ethyl cellulose, Carbopol 934-p, Calcium Chloride, Amaranth, all were Laboratory grade chemicals obtained from S.D Fine chemicals, Mumbai.

Methods:

Preformulation Studies:

Construction of Chlorhexidine Calibration curve in pH 6.8 phosphate buffer:[4]

Two stock solutions A&B were prepared. From stock solution, appropriate aliquots were pipetted out into different volumetric flasks and volumes were made up to 10 ml with 6.8pH phosphate buffer solution to get drug concentrations of 1,2,3,4 and 5µg/ml. The absorbencies of these drug solutions were estimated at λ_{max} 260nm against a blank of 6.8pH phosphate buffer solution. This procedure was performed in triplicate to validate the calibration curve. The absorbance values are summarized in table and a calibration curve was plotted between drug concentration and absorbance.

FTIR Studies: [4,5]

The infrared absorption spectra of pure drug, pure polymer and physical mixture of polymer and drug were performed for polymer drug interaction studies between 4000 $cm^{-1}$to 400 $cm^{-1}$by KBr pellet method.

Formulation of Sodium Alginate beads of Aloevera Gel & Chlorhexidine

1. Gel Collection & Stabilization:[6]

Aloevera leaves were cut and collected from the surroundings and neighborhood of Ghatkesar. Leaves were properly cleaned and air dried. Gel is collected by cutting the leaves and making various incisions. Upon cutting, there is a maximum of six hours to stabilize the active ingredients within the gel and leaf. When exposed to air the gel rapidly oxidizes, decomposes and loses much of its biological activities. Various patented methods are known for stabilization of the gel. In the heat treatment processing, sterilization is achieved by subjecting the aloe liquid obtained from the activated carbon treatment to pasteurization at high temperature. The Aloe-vera Gel is stabilized by heating at 65°c for 15min, cooled to filter and store it at cool temperature in refrigerator.

General method of Preparation of sodium alginate beads:

Prepare Sodium Alginate Solution: Dissolve sodium alginate powder in water to form a solution. The concentration can vary depending on the desired bead properties.

Prepare Aloe Vera Gel: Extract or obtain aloe vera gel. Ensure it's clean and free from any contaminants.

Alginate Solution and Aloe Vera Gel: Combine the sodium alginate solution with the aloe vera gel. The ratio will depend on the desired composition and properties of the beads.

Prepare Calcium Chloride Solution: Dissolve calcium chloride in water to create a cross- linking solution. Calcium chloride will ionically cross-link the alginate polymer, forming the beads.

Drop or Extrude the Mixture into Calcium Chloride Solution: Use a dropper or extrusion method to form droplets or beads of the alginate-aloe vera mixture into the calcium chloride solution. The calcium ions in the solution will cause the alginate to gel and form beads.

Allow Beads to Harden: Let the beads sit in the calcium chloride solution for a specific period to allow them to fully cross-link and harden.

Rinse and Dry: Once the beads have formed, rinse them with water to remove excess calcium chloride. Then, dry them either by air drying or using a gentle drying method.

Storage: Store the dried beads in an airtight container until ready for use.

Preparation of Aloe vera Gel alginate beads: [6,7]

Aloe gel was collected by making incision in mid of the leaves. Weigh 300 mg of sodium alginate and dissolve in 10 ml of distilled water and keep it aside for 75min until it swells completely. Add 2gm of Aloe vera gel, mix at 1000 rpm using magnetic stirrer (remi India) for 15min. This was then extruded via syringe (no-22) into 5% calcium chloride solution with gentle agitation at 37°C. The formed beads were allowed to

stand for 45 min in the solution to allow for curing time then separated by filtration through Whatman filter paper (size 0.45 mm) and washed again using petroleum ether to remove excess calcium chloride and other impurities and air dried for 24hrs and stored for further preparation.

Table 1: Formulation of Aloe vera Gel based sodium alginate beads and final Gel formulation

Formulation	F1	F2	F3	F4	F5	F6
Drug (%)	4	4	4	4	4	4
HPMC (Gm)	0.25	0.5	0.75	1.0	1.25	1.5
Sodium Alginate(gm)	0.3	0.3	0.3	0.3	0.3	0.3
Ethyl Cellulose (Gm)	3.0	2.5	2.0	1.5	1.0	0.5
Aloe Vera Gel (Gm)	2	2	2	2	2	2
Carbopol 934p(Gm)	2	2	2	2	2	2
Calcium Chloride (%W/V)	5	5	5	5	5	5
Amaranth	q.s	q.s	q.s	q.s	q.s	q.s

The formulation has been designed based on the references, dose of the drug Chlorhexidine for topical formulations is 4%, Aloe vera Gel's weight is constant in all the formulations i.e. half of the drug to avoid changes in the formulation. Carbopol 934p is the gelling agent used to get the perfect gel structure and texture for topical application. Sodium Alginate is constant to prepare alginate beads and Ethyl cellulose was employed 0.5-3.0% conc as Aloe vera is hydrophilic and for intact formation of alginate beads without dispersion. HPMC in the ratios of 0.25 up to 1.5 to control the release of Hydrophilic gel based on handbook of Pharmaceutical Excipients.

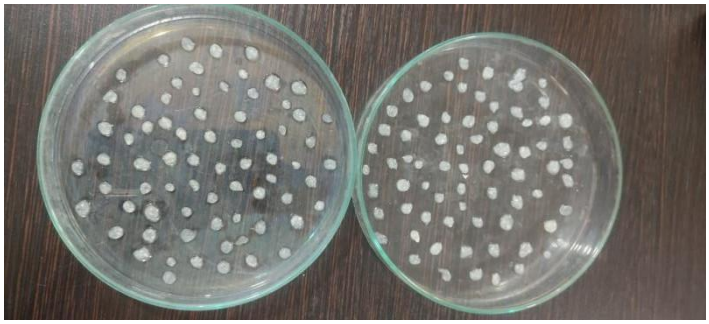

Fig 1: Sodium Alginate beads containing Aloe vera Gel & Chlorhexidine

Fig 2: Aloe vera gel and Chlorhexidine sodium alginate beads incorporated Gel.

Evaluation Studies

1. Particle Size Analysis [4,7]

The mean particle size of the various formulations (F1 to F6) of microbeads were obtained in the range between 1.33 ± 0.06 mm and 1.45 ± 0.03 mm. In fixed concentration of sodium alginate and calcium chloride and increases in the coating polymer

concentration results increases in diameter of microbeads (F1 to F6)

2. pH: [4,8]

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

3. Entrapment efficiency:[8]

The alginate beads prepared were washed with buffer to remove externally entrapped drug and they are subjected to centrifugation at 1000rpm for 15min. This process breaks the alginate beads and releases the drug into the buffer solution. Supernatant is cleared and the solution is collected. Samples are subjected to determination by UV spectroscopy after suitable dilution at 260nm.

4. Spreadability:[9]

One of the criteria for a topical formulation to meet the ideal qualities is that it should possess good spreadability. It is the term expressed to denote the extent of area to which formulation readily spreads on application to skin or affected part. The therapeutic efficacy of a formulation also depends upon its spreading value. To determine the spreadability of formulation, 0.5 g of gel was placed within a circle of 1 cm diameter pre-marked on a glass plate of 20 × 20 cm, over which a second glass plate was placed. A weight of 500 g was allowed to rest on the upper glass plate for 5 min. The increase in the diameter due to gel spreading was noted.

5. Viscosity:[9]

Viscosity of the gel formulations (F1 -F6) were studied using Brookfield viscometer. The gel in weighed quantity was taken in a beaker and the spindle was inserted into the gel formulations and allowed rotate to monitor the viscosity.

6. Diffusion study:[9]

Drug diffusion study was conducted using Franz diffusion cell. The Gel was placed in a packed cellophane membrane closed on either side. The locked gel was place in between the receptor and donor compartment. pH 6.8 buffer solution of 14ml and 3ml was filled in receptor and donor compartment respectively. The diffusion cell was placed on magnetic stirrer at a temperature of 37±0.5°C and drug diffusion from gel formulations was studied at regular intervals of time by collecting 3ml samples and measuring the absorbance using UV-Spectrophotometer at 260nm.

7. Stability studies:[4]

The accelerated stability studies were conducted as per ICH guidelines. India falls under Zone IV based on which the temperature and humidity conditions were applied. The formulation of F3 was evaluated for stability studies which was stored at 30˚C 75% RH for 30 days and evaluated for their physical appearance, drug content and invitro disintegration time and % drug release at the end of 30 days.

RESULTS AND DISCUSSION:

Preformulation studies:

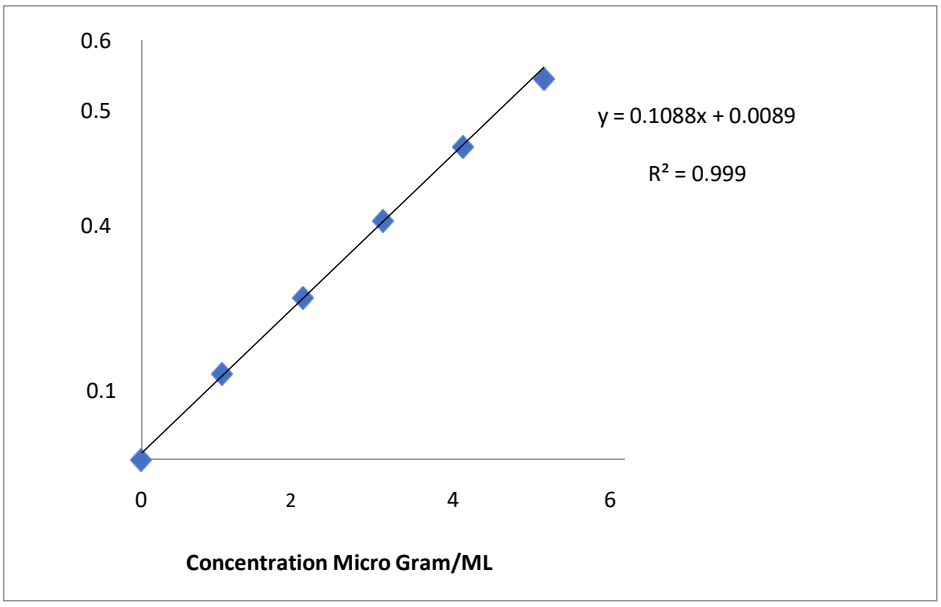

Fig 3: Calibration data of Chlorhexidine in 6.8pH phosphate buffer

FTIR Studies:

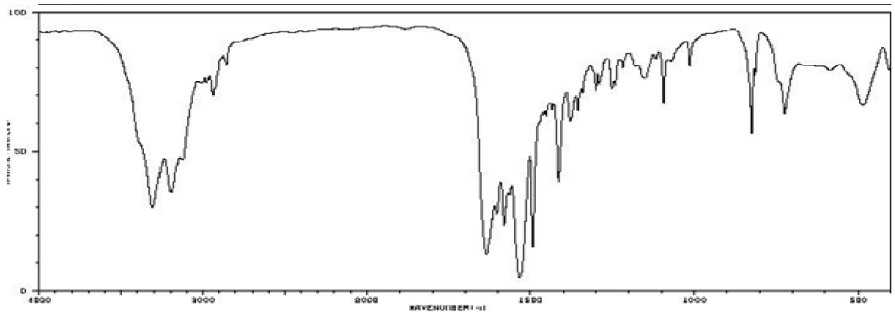

Fig 4: FTIR Spectra of Pure drug of Chlorhexidine

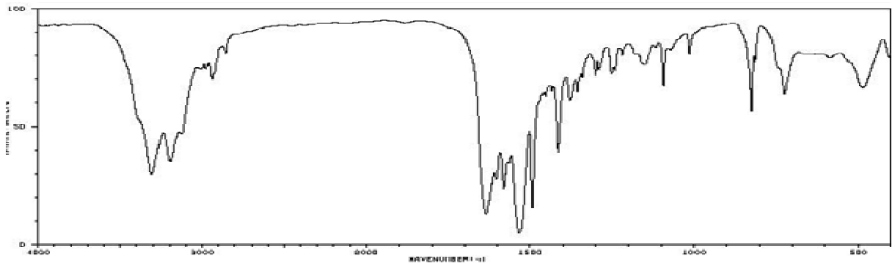

Fig 5: FTIR Spectra of Optimised formulation (Drug and excipients) of Chlorhexidine gel

Table 2: IR Interpretation Data of Chlorhexidine pure drug and Optimized formulation

S. No.	Literature value	Observed value	Inference
1	3500-3200	3380.126	-NH
2	1670-1640	1662.918	C=C Aromatic
3	1640-1550	1529.157	N-H Bending
4	1300-1000	1072	Aliphatic C-N
5	800-600	742.734	C-Cl

As there was no change in the spectra and its Inference observed for both pure drug of Chlorhexidine and chlorhexidine with excipients it shows us that there was no interaction found and there is compatibility between the drug and excipients.

Table 2: Post formulation evaluation parameters of Chlorhexidine Gel containing aloe vera alginate beads

Formulation	Particle Size (mm)	pH	Spreadability	Viscosity (cps)	Entrapment efficiency (%)
F1	1.33±0.0004	5.5±0.001	Good	1200±0.0011	73±0.0002
F2	1.32±0.0002	6.0±0.002	Moderate	1400±0.0011	85±0.0003
F3	1.40±0.0003	5.8±0.0009	Excellent	1100±0.0021	94±0.0001
F4	1.45±0.00012	6.2±0.0021	Fair	1600±0.0013	80±0.0005
F5	1.39±0.0002	5.7±0.001	Good	1300±0.0016	82±0.0004
F6	1.41±0.0005	5.9±0.001	Excellent	1500±0.0012	88±0.0002

Post formulation parameters show that particle size is optimum, pH of the formulations is matched to skin pH that helps in penetration of Gel. Spreadability was fair to excellent, Viscosity is 1100-1600cps and entrapment efficiency ranges between 73- 94%. Based on these parameters formulation F3 was considered as optimum formulation for diffusion studies.

Table 3: Diffusion study of Chlorhexidine Gel containing Aloe vera Gel and Sodium Alginate beads

Formulation	% Cumulative Drug Diffusion / Time (Hr)						
	0.5	1	1.5	2	2.5	3	3.5
F1	10±0.0001	21±0.0015	34±0.0011	47±0.0005	58±0.0007	63±0.0017	70±0.0033
F2	12±00012	23±0.0023	39±0.0005	51±0.0013	63±0.0008	72±0.0022	83±0.0025
F3	15±0.0011	27±00018	42±0.0007	60±0.0024	73±0.00019	85±0.0034	92±0.0013
F4	17±0.0022	29±0.0021	40±0.0009	58±0.0026	68±0.0011	75±0.0023	79±0.0009
F5	11±0.0031	22±0.0031	37±0.0022	59±0.0014	64±0.0025	73±0.0018	80±0.0015
F6	14±0.00 24	28±0.0014	40±0.0015	54±0.0022	69±0.0016	77±0.0017	85±0.0022

The Inference of Drug diffusion studies show the drug release from various formulations between 70-92% within 3.5hrs. The maximum drug diffusion was shown by F3 i.e. 92% in 3.5hrs, hence it is considered as best formulation.

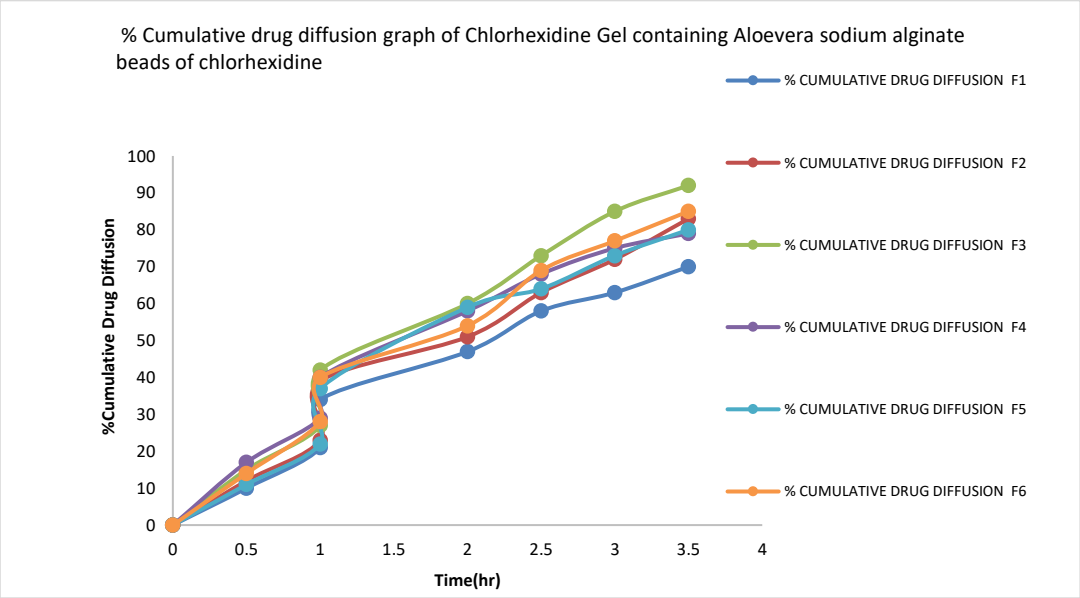

Fig 6: %Cumulative drug diffusion graph of Chlorhexidine Gel containing Aloe vera sodium alginate beads of chlorhexidine

Stability studies:

Table 4: Stability data of Chlorhexidine gel at 40˚C / 75% RH for 30days

Time in months	Formulation F3 stored at 40˚C / 75% RH			
	Physical Appearance	Drug content (%)	Spreadability	% Drug release
Initial	Smooth & Elegant	94.86±0.0004	excellent	92.15±0.0012
After 1 Month	Smooth &Elegant	94.53±0.0003	excellent	91.15±0.0011

CONCLUSION:

Sodium Alginate beads are formed, the formulated chlorhexidine-aloe vera-sodium alginate beads incorporated gel holds promise as a potential topical antimicrobial agent with sustained release properties, suitable for various pharmaceutical and therapeutic applications. Further studies including in vivo evaluations are warranted to validate its clinical efficacy and safety.

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REFERENCES:

1. Garcia-Orue I, Gainza G, Gutierrez FB, Aguirre JJ, Evora C, Pedraz JL, Hernandez RM, Delgado A and Igartua M, Novel nanofibrous dressings containing rh EGF and Aloe vera for wound healing applications. Int J Pharm 2017;523: 556–566.
2. Kataria S, Middha A, Sandhu P, Bilandi A and Kapoor B: Microsphere: a review. IJRPC 2011; 1(4): 1184-1198.
3. Chirag Upadhyay, Vibha, Devender Pathak, Mayank Kulshreshta, preparation and Evaluation of different herbal gels synthesized from Chinese medicinal plants as an anti-microbial agent, Pharmacological Research - Modern Chinese Medicine, December 2023, vol 9, 100313.
4. Indian Pharmacopeia, Ministry of Health and Family Welfare. Ghaziabad, India: The Indian Pharmacopeia commission. 2014.
5. Gurdeep R Chatwal and Sham K Anand. Instrumental methods of Chemical Analysis. Himalaya Publishing House, Mumbai. 2011; 2.44.
6. Katarzyna Bialik-Was, Konstantinos N. Raftopoulos, Krzysztof Pielichowski, Alginate Hydrogels with *Aloe vera*: The effects of Reaction Temperature on Morphology and Thermal Properties, Materials (Basel), Feb 2022; 15(3):748.
7. Alfred Martin, Physical Pharmacy, B.I. Waverly Private Limited,New Delhi 4th Edition 431,444-448.
8. B.k pawan Jalwal, Formulation and evaluation of Chlorhexidine gluconate topical gel, March 31, 2015**,** Corpus ID: 199080665.
9. Guru Mohanta, N. Subramanian, R.Manvalan, Y V Rao; Formulation and evaluation of film forming chlorhexidine gluconate gels, January 2000, INDIAN DRUGS 37(12):561-565.