ejpmr, 2017,4(11), 420-423

SJIF Impact Factor 4.161

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

DEVELOPMENT AND EVALUATION OF SILVER SULPHADIAZINE LOADED SODIUM ALGINATE GELATIN FILM FOR WOUND DRESSING APPLICATIONS

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Article Received on 01/09/2017 **Article Revised on 22/09/2017** **Article Accepted on 13/10/2017**

ABSTRACT

Aim of this study was to develop novel bio medicated film for wound dressing applications. Film of gelatin and sodium alginate loaded with silver sulphadiazine were successfully prepared by solvent casting method. The formulations were subjected to various physico chemical evaluations such as weight variation, surface pH, folding endurance, moisture evaluation studies, biodegradability and in vitro drug release studies. All the prepared films were found to be transparent, flexible with smooth surface. The results of physicochemical characteristics of Medicated films were satisfactory with respect to weight variation, surface pH, folding endurance, and moisture loss and moisture uptake studies. The drug entrapment was found to be in acceptable range for all the formulations, indicating uniform distribution of the drug. Films prepared using sodium alginate and gelatin showed satisfactory biodegradability. Thus, Gelatin-SA wound dressing system containing silver sulphadiazine could be a good polymeric membrane candidate in wound care.

KEYWORDS: Medicated film, biodegradability, wound healing.

1. INTRODUCTION

A wound is defined as a disruption in the continuity of the epithelial lining of the skin or mucosa resulting from physical or thermal damage. According to the duration and nature of healing process, the wound is categorized as acute and chronic. An acute wound is an injury to the skin that occurs suddenly due to accident or surgical injury. Chronic wounds on the other hand fail to progress through the normal stages of healing and cannot be repaired in an orderly and timely manner. Wound healing is a dynamic and complex process of tissue regeneration and growth progress through four different phases (i) the coagulation and haemostasis phase (immediately after injury); (ii) the inflammatory phase, (shortly after injury to tissue) during which swelling takes place; (iii) the proliferation period, where new tissues and blood vessels are formed and (iv) the maturation phase, in which remodeling of new tissues takes place. With the advancement in technology, currently, different types of wound dressing materials are available for all types of wounds.[1]

The ideal wound dressing accelerates the healing process, prevents infection, and restores the structure and function of the skin. Historically, the first documentation of wound care can be found in the ancient Sumerians who used to apply poultices of mud, milk, and plants to wounds. The Egyptians prepared plasters of honey, plant fibers, and animal fats as bandages for the wounds. The most important advances in the field came with the development of microbiology and cellular pathology during the 19th century. One of the main contributions was the discovery in the 1960s that keeping a wound moist accelerates the healing process. This became a key parameter in the design and development of wound dressings. However, wound dressings should satisfy other essential requirements for encouraging healing, including: i) absorbing excessive exudates from the wound bed, ii) providing thermal insulation, protecting the wound bed from mechanical trauma and bacterial infiltration, iii) allowing gaseous and fluid Passive wound dressings provide protection of the wound bed from mechanical trauma exchanges, iv) being removable without trauma, and v) being nontoxic and nonallergenic.[2]

Alginate is a natural heteroglycan formed by the combination (1,4)-b-D-mannuronic acid and (1,3)-a-L-guluronic acid and obtained from a brown sea weed. Sodium alginate is water soluble, biocompatible, biodegradable polyelectrolyte which has been used as a natural polymer in various applications related to tissue engineering, drug delivery, wound dressing etc. Gelatin has been studied as a biodegradable polymer not only for its film forming properties but also for its availability and economical advantages over other synthetic biopolymers. Gelatin has been used in the food, pharmaceutical, biomedical, and photographic industries. In biomedical

applications, gelatin has been developed for wound dressings, absorbent pads for surgical purposes, microspheres, and capsules.[3]

Thiswork is focused on the formulation and evaluation of silver sulphadiazine loaded Sodium alginate/Gelatine (SA/G) film for wound dressing applications.

2. MATERIALS AND METHODS

2.1. Materials

Silver Sulphadiazine was obtained as a gift sample from Galentic India Pvt.Ltd Mumbai. Sodium alginate (SA) and gelatin was purchased from Nice chemicals, Kochi. Lysozyme was obtained from Yarrow Chem Pvt. Ltd, Mumbai. All other agents were analytically pure. The polymer and the solvent were used without further purification

2.2 Fabrication of Medicated Film[4]

Wound healing film was prepared by solvent casting method where using Sodium alginate and gelatin as polymers and propylene glycol or polyethylene glycol as plasticizer. For preparation of polymer mixture film, sodium alginate and gelatin were dissolved in distilled water with continuous stirring to avoid lump formation. Plasticizer in different amount and silver sulphadiazine (1%w/v) were then added and allowed to mix homogenously for 1 h using remi stirrer at 100 rpm and poured on Teflon petriplate. The resulting solution was kept in vacuum oven till air entrapped was removed from the solution. The solution was allowed to dry at 30°C for 6 h followed by drying in hot air oven at 45°C for 24 h.

Table1: Formulation table for the.

	F1	F2	F3	F4	F5	F6	F7
Drug(mg)	100	100	100	100	100	100	100
Sodium alginate(mg)	500	450	400	350	300	250	200
Gelatin(mg)	300	350	400	450	500	550	600
PEG 400(ml)	0.15	0.15	0.15	0.15	0.15	0.15	0.15
Water	q.s	q.s	q.s	q.s	q.s	q.s	q.s

Medicated Film.

2.3 Evaluations of the Medicated film

2.3.1 Physical appearance

All the films were visually inspected for color, clarity, flexibility and smoothness.

2.3.2 Weight Variation.[5]

Individual batches of films of size (2×2 cm²) was cut exactly at three different places and the weight of each film was taken on an electronic balance and the average weight and standard deviation were calculated.

2.3.3 Surface pH[6]

The surface pH of films was determined in order to investigate the possibility of any adverse effects in vivo. The films (1cm X 1 cm) was allowed to swell in closed petri dish at room temperature for 30 minutes in 5ml of distilled water. Swollen films was removed and placed under digital pH meter to determine the surface pH.

2.3.4 Folding endurance[6]

Folding endurance was determined to find the flexibility of films which is essential for the handling, comfort and secured application of films on the wound. Folding endurance was measuredby folding the films at the same place till it breaks. The number of times it could be folded at thesame place without breaking gave the exact value of folding endurance.

2.3.5 Percentage moisture content[6]

The prepared films were weighed individually and kept in a desiccator containing calcium chlorideat room temperature for about 24 hours. The films were weighed repeatedly until they showed aconstant weight. Values for the percentage of moisture content were calculated using the formula.

$$\text{Percentage of moisture content} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Final weight}} \times 100$$

2.3.6 Percentage moisture uptake.

The weighed films were kept in a desiccator at room temperature for 24 hours and then exposed to 84% RH using a saturated solution of potassium chloride. The films were weighed repeatedly until they showed a constant weight. Values for the percentage of moisture uptake were calculated using the formula.

$$\text{Percentage of moisture uptake} = \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \times 100$$

2.3.7 Drug content estimation

Films were cut into 2 × 2 cm and taken in a 100 ml standard flask. Dissolved the contents in ammonia solution and made up to the volume with distilled water and subjected to continuous shaking in a shaker for 3 hours. After proper dilution, the absorbance was measured at 254 nm using a UV Visible Spectrophotometer.

2.3.8 Biodegradability Test[7]

The Invitro degradation of Medicated films (2x2cm) was carried out in 1ml phosphate buffersolution (PBS, PH 7.4) at 37°C containing 1.5 µg/ml lysozyme. The

concentration of enzyme was chosento correspond to the concentration in the human serum. Briefly; films of known dry weights weresterilized by autoclaving (120°C, 20 min) and incubated in the lysozyme solution with gentle mechanicalagitation during the period of study. The lysozyme solution was refreshed daily to ensure continuous enzyme activity. The samples were withdrawn at definite time intervals from the medium, rinsed with distilled water, dried under vacuum and weighed. The in vitro degradation was expressed as percentage of weight loss of the dried films on every alternate day during the lysozyme treatment. To separate between enzymatic degradation and dissolution, control samples were stored under the same conditions as described above, but without the addition of lysozyme.

2.3.9 Cumulative Drug Release

The cumulative drug release study was done simultaneously with biodegradability test. The drug content in the replaced enzymatic media of the biodegradability test was estimated spectrophotometrically at 254 nm.

3. RESULTS AND DISCUSSION

3.1 Physical appearance

All the drug loaded films were found to be transparent, flexible with smooth surface.

3.2 Weight Variation

Weight variation studies were conducted on all the formulations and reported in table. Results showed that mean weight of the films ranged from 51.84±1.54 mg to 60.08±0.43 mg. The weight uniformity data for all the formulations showed that there was no significant difference in the weight of individual formulations from the average value and the variations were within low standard deviation. Low deviation value in weight variation measurements ensured uniformity of the films.

3.3 Surface pH

The surface pH of all the formulations ranged from 6.28±0.27 to 7.31±0.06. Since the surface pH of films was around the neutral range, there will not be any kind of irritation or allergic reaction on the skin, wound and surrounding area.

3.4 Folding endurance

In order to evaluate the brittleness/flexibility, the films were subjected to foldingEndurance test. The values were in between 337±0.96 to 459±0.69 folding. This revealed that the prepared films were having capacity to withstand the mechanical pressure along with good flexibility.

3.5 Moisture Content, Moisture uptake

Moisture content and moisture uptake studies were conducted on all the formulations and reported in table.Moisture content and moisture uptake studies indicated that the increasing conc. of sodium alginate may be attributed to the hygroscopic nature of the polymeric films.

3.6 Drug entrapment

The percentage drug entrapped in various formulations ranged from 90.23% to 97.75%. All the formulations showed the presence of high drug entrapment. The drug entrapment was found to be in acceptable range for all the formulations, indicating uniform distribution of the drug.

3.7 Biodegradability test and cumulative drug release

The in vitro degradation study revealed that the polymers can be degraded by Lysozyme, which indicated their controllable biodegradability.

Table2: Physico chemical evaluations of Film

Formulation Code	Weight Variation (mg/4cm^2)	Surface pH	Folding endurance	Moisture Content (%)	Moisture Uptake (%)	Entrapment efficiency(%)
F1	51.84±1.54	6.28±0.27	337±0.96	5.01±0.98	9.66±0.64	93.38
F2	53.24±1.24	7.21±0.09	350±1.85	4.90±1.12	10.03±1.75	93.59
F3	60.08±0.43	6.73±0.17	397±4.51	3.96±0.85	8.11±0.75	94.41
F4	55.84±0.57	6.81±0.26	442±3.04	2.55±1.05	9.67±0.89	97.75
F5	54.08±0.43	6.92±0.11	459±0.69	3.90±1.31	6.22±1.54	96.82
F6	51.12±1.15	7.31±0.06	415±2.21	2.92±0.95	6.89±0.56	96.12
F7	51.53±1.52	6.72±0.19	338±3.25	2.11±1.16	5.28±0.91	90.23

Table 3: Results of Biodegradation Study.

Formulation Code	Percentage (%) weight loss at different days.				
	2 nd day	4 th day	6 th day	8 th day	10 th day
F1	18.46	34.18	50.53	69.54	86.13
F2	17.80	33.10	49.54	64.08	80.39
F3	19.27	33.72	50.12	65.33	82.73
F4	18.35	27.77	45.41	60.46	72.81
F5	14.80	23.10	46.54	62.08	72.39
F6	11.27	23.72	44.12	60.33	71.73
F7	14.35	26.13	43.89	58.97	70.55

Table 4: Percentage Cumulative Drug Release of film.

Formulation code	Time in days						
	1	2	3	4	5	6	7
F1	13.73	28.21	44.97	57.4	71.55	85.03	97.68
F2	15.24	28.81	39.46	52.01	60.39	78.54	91.25
F3	14.39	25.87	40.63	55.67	67.8	81.07	92.83
F4	11.99	20.96	33.02	47.56	60.68	70.56	82.8
F5	9.88	22.45	32.65	45.67	58.82	70.77	78.03
F6	12.45	23.48	41.61	53.18	63.88	77.64	87.56
F7	8.34	18.33	30.82	45.72	60.77	72.07	81.72

4. CONCLUSION

Medicated films of silver sulphadiazine was successfully developed and evaluated. All the prepared films were found to be transparent, flexible with smooth surface. The results of physicochemical characteristics of Medicated films weresatisfactory with respect to weight variation, surface pH, folding endurance, and moisture loss andmoisture uptake studies. The drug entrapment was found to be in acceptable range for all theformulations, indicating uniform distribution of the drug. Films prepared using sodium alginate and gelatin showed satisfactory biodegradability. The in vitro drug release studies showed formulation F1 has high drug release as compared to other formulations.

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