ISSN 2580-4936

Health Notions

Published by: Humanistic Network for Science and Technology

http://heanoti.com/index.php/hn

Volume 2 Number 9
September 2018

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Health Notions
ISSN 2580-4936
Published by
Humanistic Network for Science and Technology

HEALTH NOTIONS

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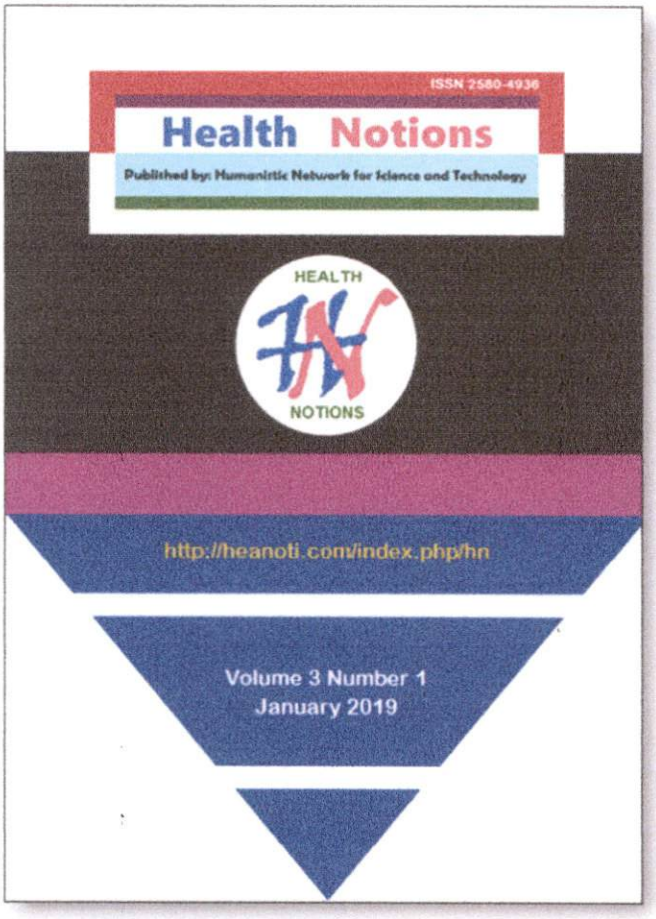

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ISSN 2580-4936
Published by
Humanistic Network for Science and Technology

Published: 2018-09-03

Research Article

Lilin Rosyanti

Optimation Ca-Alginate Beads as Drug Reservoir in the Patch System for Model Anti-Inflammatory Drug

Esti Hendradi, Isnaeni Isnaeni, Rifaatul Mahmudah

Oral Hygiene Behavior and Periodontal Disease Status of Fishpond Community

Narita Ajeng Loviana, Ristya Widi Endah Yani

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RESEARCH ARTICLE

URL of this article: http://heanoti.com/index.php/hn/article/view/hn20908

Optimation Ca-Alginate Beads as Drug Reservoir in the Patch System for Model Anti-Inflammatory Drug

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ABSTRACT

The aim of this study was to optimize the use of Ca-Alginates beads as a drug reservoir in the patch system with and without freeze-drying process. Meloxicam, an anti-inflammatory non-steroidal drug, was used as a drug model. Ca-alginate beads were prepared by ionic gelation method using polymer alginate and cross-linker $CaCl_2$. The beads were evaluated for its melting temperature, FTIR spectra, and entrapment efficiency. The FTIR study showed the loss of guluronic peaks of alginate caused by a cross-linking process with Ca^{2+}, characteristics peaks of meloxicam still appeared indicating the compatibility of the drug with the polymers used. The using Ca-alginate beads without freeze-drying process as a drug reservoir resulted in a very wet patch that was difficult to dry, cracked surface, and pharmaceutically not acceptable. Meanwhile, patch using Ca-alginate beads with the freeze-drying process as a drug reservoir demonstrated satisfactory characteristics with minimum weight variation among the patches that lead to giving uniformity in the drug content.

Keywords: Ca-alginate, Freeze-dry, Patch, Meloxicam, Transdermal delivery

INTRODUCTION

Background

Ca-alginate beads formed of complexation of polymer alginate with ca^{2+} cation. Alginate is a natural polymer derived from brown algae that widely used in food, biomedical, and pharmaceutical applications because of its biocompatible and biodegradable properties. Ca-Alginate beads or Alginate hydrogels were safe and cheap to prepare and can be used in a variety of applications. Ca-alginate beads have been used for drug delivery such as the parenteral delivery of chemotherapeutics and topical drug applications such as wound healing dressings[(1)]. Ca-alginate beads may act as not only the drug transporters but also the reservoir that releases an active ingredient over an extended period of time to maintain effective drug concentration in the skin and at the same time, reducing undesired side effects[(2)].

Meloxicam (4-hydroxy-2-methyl-N-(5-methyl-2-thiazoyl)-2H-1, 2-benzothiazine-3-carboxamide-1, 1-dioxide) is a non-steroidal anti-inflammatory drug (NSAID) that shows efficacy for reducing pain and inflammatory symptoms and has definite activity in treating osteoarthritis, rheumatoid arthritis and ankylosing spondylitis [(3)]. Meloxicam inhibits the cyclooxygenase-2 (COX-2) isozyme and shows similar efficacy but lower toxicity than the other NSAIDs [(4,5)].

Meloxicam has low toxicity for oral administration but it can cause frequent gastrointestinal side effects such as gastrointestinal perforation and ulceration and/or bleeding. Meloxicam 15 mg for 14 and 28 days had higher endoscopy scores compared to 7.5 mg meloxicam, suggesting that long-term therapy and high doses of it can induce more significant gastrointestinal side effects [(6)]. So, it required an alternative route which could avoid the disadvantages.

One promising method is to deliver drug via skin (Transdermal). Transdermal drug delivery system (TDDS) is an innovative technique for the application on the skin to achieve local and or systemic effects. It has several advantages over other routes of drug delivery like provides convenient and painless, enhanced and controlled therapeutic responses and avoid adverse effects of oral administration[(7)]. So it can deliver a drug directly to the disease site in order to maximize local effects with minimum systemic activity.

The aim of this study was to optimation the use of Ca-Alginate beads as a drug reservoir in the patch system for an anti-inflammatory drug that can achieve sustained release anti-inflammatory activity. Moreover, to provide a transdermal dosage form which able to reduce the frequency of dosing so that it can be applied to other drugs that have a short half-time.

METHODS

The calibration curve was prepared with phosphate buffer saline pH 7.4 in the concentration range 1-10 µg/ml. The absorbance was measured at 363 nm using Uv-Vis spectrophotometer and recorded, then concentration vs absorbance values was plotted. Ca-Alginate beads were prepared using the ionotropic gelation technique. Meloxicam was dispersed in an aqueous solution of 1% w/v sodium alginate with continuous stirring. The polymer-drug solution was sprayed into a beaker containing 4% w/v solution of calcium chloride with continuous stirring at 1000 rpm. Beads were collected/filtered using Whattman filter paper and washed out using aqua demineralized. Ca-alginate beads that have been washed can be directly applied over the backing layer as a drug reservoir and dried using an oven for 4 hours, then the HPMC polymer as rate controlling membrane was applied to it and dried again for 2 hours.

Other formulas were made with the same method but undergo a freeze-drying process after washing and resulted in a dry powder ca-alginate beads form. The Ca-alginate beads powder then dispersed in HPMC solution formed a patch similar to a microreservoir type patch.

Ca-alginate beads were evaluated for its melting temperature, FTIR spectra and entrapment efficiency meanwhile the patches were examined visually and inspected for smoothness, color, and odor. Moisture content was determined by placed patches in a desiccator containing silica as a desiccant and weighing each patch individually each every 30 minutes. Percent moisture loss is a measure of moisture content. Drug content evaluated by dissolved patches in a phosphate buffer saline pH 7.4. The solutions were stirred for 7 h and filtered. Meloxicam concentration was determined using Uv-Vis spectrophotometer against a blank prepared similarly without meloxicam.

RESULTS

Calibration Curve of Meloxicam

A standard curve ranging from 1-10 µg/ml with phosphate buffer saline pH 7.4 at 363 nm was found to be linear with y=0.0549x and R2=0.9994 as shown in Figure 1.

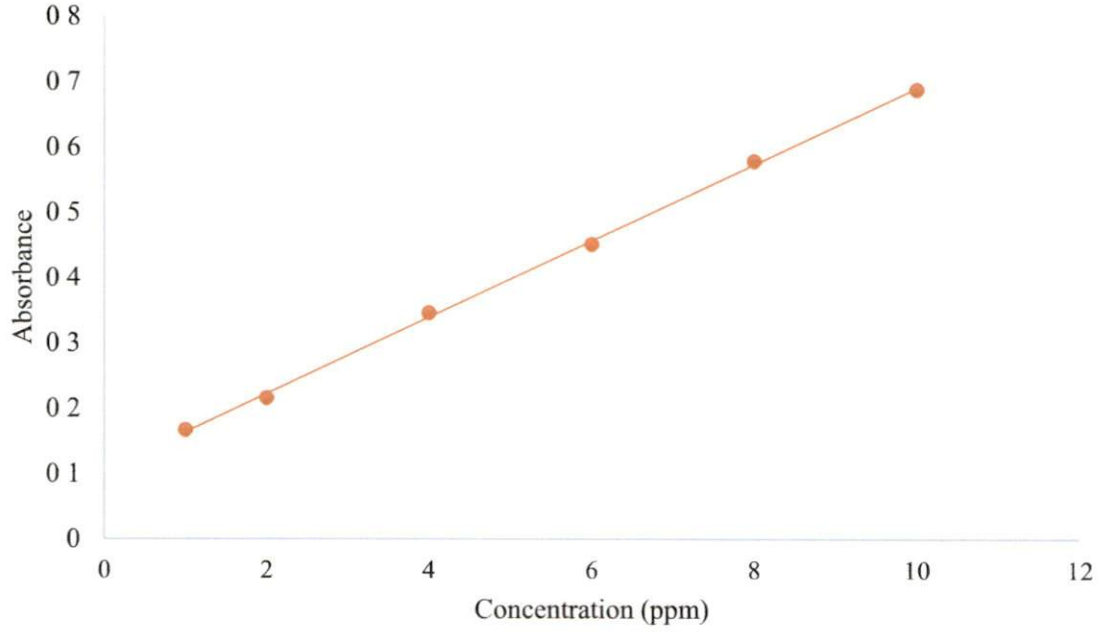


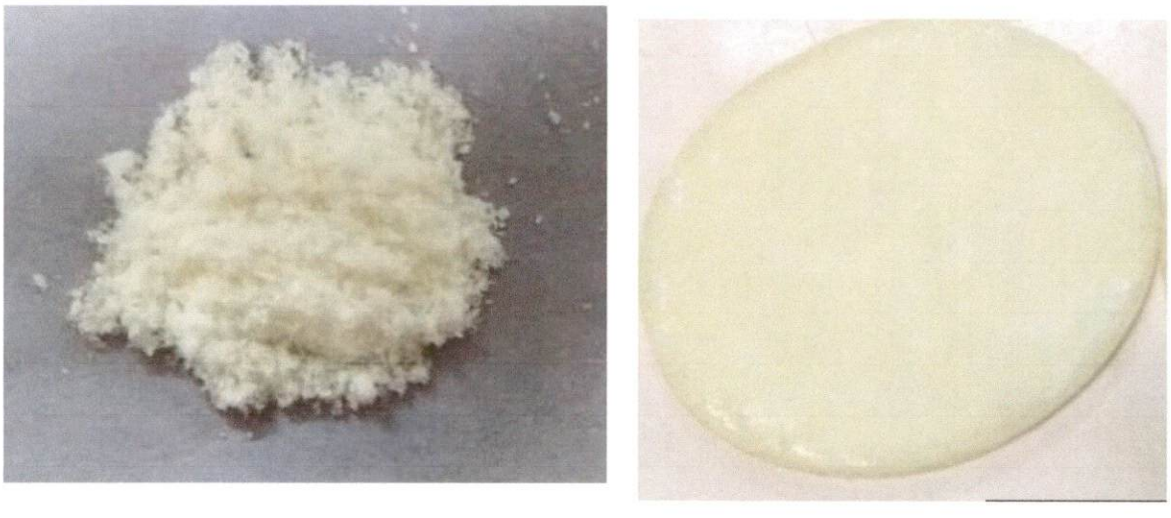
Figure 1. Standard calibration curve of meloxicam.

Wet Ca-Alginate Beads and Dry Powder Ca-Alginate as a Drug Reservoir

The appearance of wet ca-alginate beads and dry powder ca-alginate was shown in figure 2 and figure 3 as well as the appearance of the patch while using wet ca-alginate beads and dry powder ca-alginate as a drug reservoir

(a) (b)

Figure 2. Wet Ca-alginate beads (a) and Patch using wet Ca-alginate beads as a drug reservoir (b).



(a) (b)

Figure 3. Dry powder Ca-Alginate beads (a) and Patch using dry powder Ca-Alginate beads as a drug reservoir.

Drug-polymer interaction study

The FTIR study and melting temperature (DTA) only carried out on dry powder ca-alginate beads. The FTIR and DTA study were presented in figure 4 and figure 5.

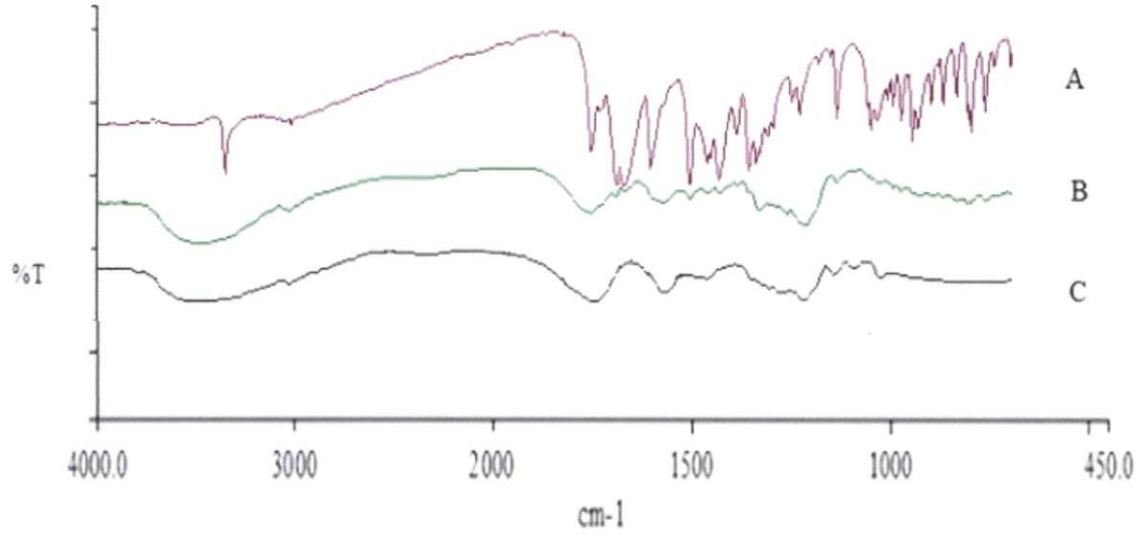


Figure 4. IR spectra of : (A) pure meloxicam; (B) meloxicam-loaded Ca-alginate beads; (C) alginate.

Organoleptic, weight and moisture content of Patch using dry powder Ca-Alginate beads as a drug reservoir

Organoleptic, weight and moisture content of patch using dry powder Ca-alginate beads as a drug reservoir were shown in table 1.

Table 1. Organoleptic observation, weight and moisture content of meloxicam patch using dry powder Ca-alginate beads as a drug reservoir.

Replication	Shape	Color	Odor	Weight (mg)	Moisture content (%)
I	Thin, slightly stiff, smooth surface texture	Yellow	Odorless	850	8.8
II	Thin, slightly stiff, smooth surface texture	Yellow	Odorless	907	8.4
III	Thin, slightly stiff, smooth surface texture	Yellow	odorless	909	9.0
Average				889	8.7
SD				0.032	0.33

Drug Content

Drug content of patch using dry powder Ca-alginate beads as a drug reservoir were shown in table 2.

Table 2. Drug content of meloxicam reservoir type patches.

Replication	Drug content (%)	Average (%)	SD
I	96.37		
II	97.28	96.37	0.14
III	95.46		

DISCUSSION

Meloxicam-loaded Ca-alginate beads were successfully prepared by ionotropic gelation method. Although only carried out on dry powder Ca-alginate beads, from the FT-IR spectra of the pure drug and polymer and meloxicam-loaded Ca-alginate beads we knew that there was interaction characterized by the shifts of wavelength and loss of guluronic fingerprint of Na-alginate caused by cross-linking reaction with $CaCl_2$. DTA thermogram (not displayed) of pure drug, polymer, and meloxicam-loaded Ca-alginate beads showed a sharp peak of melting temperature about 255,6 C for meloxicam, 193 C for alginate, but no related peak was observed for meloxicam-loaded Ca-alginate beads formulation. These result suggested that drug was totally entrapped in polymer and there was a new system formed that has a new melting temperature (165 C).

From figure 2 we knew that the using Ca-alginate beads without freeze-drying process (wet Ca-alginate beads) as a drug reservoir resulted in a very wet patch that was difficult to dry, cracked surface, and pharmaceutically not acceptable. The patch takes a long time to dry and when it was dried, the surface was cracked and rough. Therefore, the next optimization was only done by using Ca-alginate beads which have been through a freeze-drying process.

All patches showed a yellow color due to meloxicam color. There were no significant differences between replication 1, 2, and 3 in visual observation as well as the weight and moisture content value. Moisture content value of the patches was found to be slightly larger than expected, it was difficult to lower the moisture content value because the patch will be very rigid. There was no problem with this because the patch also required a certain amount of water to increase the hydration of the skin.

The Drug content result were shown in table 2. Based on one-way ANOVA, there were no significant differences in drug content between the replication ($p > 0,05$). Maybe the good content uniformity between the replication formula due to minimum weight variation among the patches that lead to giving uniformity in the drug content. These results indicated that the use of dry powder Ca-alginate beads as drug reservoir has the potential to formed a patch with minimum weight variability and uniform drug content.

CONCLUSION

A dry powder Ca-alginate beads were can be used as a drug reservoir for patch system. The drug can be trapped well in the system and the patches demonstrated satisfactory characteristics with minimum weight variation among the patches that lead to giving uniformity in the drug content.

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