Available online on 15.06.2023 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

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Research Article

Formulation and evaluation of Epsom salt-based gel to reduce osteoarthritis pain

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Article Info:

Article History:

Received 24 March 2023
Reviewed 16 May 2023
Accepted 03 June 2023
Published 15 June 2023

Cite this article as:

Santosa A, Ratri R, Isnaini N, Astuti IY, Formulation and evaluation of Epsom salt-based gel to reduce osteoarthritis pain, Journal of Drug Delivery and Therapeutics. 2023; 13(6):112-17

DOI: http://dx.doi.org/10.22270/jddt.v13i6.6114

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Abstract

Epsom salt as Osteoarthritis (OA) pain therapy has been limited to compresses, foot soaks, and baths. Many studies have examined Epsom salt to reduce pain, especially in OA, but Epsom salt formulation in gel form has never been tried, so it needs in-depth scientific evidence. This study aims to formulate an Epsom salt gel and test its effectiveness in reducing pain for OA patients. This is a true-experimental study with a completely randomized design. A total of 22 respondents with OA were included in the trial. In this study, each respondent received five treatments randomly (administration of pure gel (Negative control); Epsom salt gel with a concentration of 2%; 2.5%; 3%, and Diclofenac sodium (Positive control). Respondents' pain scale was assessed at the beginning and the end of each treatment as an outcome in this study. The data were analyzed using One-Way ANOVA and Tukey HSD. Epsom salt gels were successfully made with 2%, 2.5%, and 3% concentrations. The formulation results have met the physical test of gel preparation (organoleptic test, homogeneity, pH, and consistency). The results of clinical trials found that all Epsom salt gel concentrations effectively reduce OA pain levels ($p<0.0001$ vs. Control negative). Epsom salt gel with a concentration of 3% has a higher effectiveness level than other concentrations ($p<0.0001$). The effectiveness of Epsom salt gel with a concentration of 3% is almost equivalent to the oral drug diclofenac sodium. In conclusion, Epsom salt gel with a concentration of 3% as a topical drug has significantly reduced OA pain levels.

Keywords: Epsom Salt Gels; Magnesium Sulfate; Pain; Osteoarthritis

INTRODUCTION

Osteoarthritis (OA) is an inflammation of the joints due to damage to the cartilage tissue.[1] OA globally reaches 300 million people, making it the 11th most debilitating disease worldwide.[2,3] Aging is a significant factor in the occurrence of OA.[4,5] Other factors of OA risks are obesity,[6] injury to the joints,[7] and heavy work that overloads the joints.[8]

One of the symptoms that OA sufferers often complain about is pain.[9] Usually, OA pain is treated through pharmacological and non-pharmacological approaches. Oral Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) are the most common and effective treatment for OA but have side effects for their users. Some non-pharmacological therapies, such as soaking, can also reduce OA pain.[10] Based on previous research, soaking the feet using warm water mixed with Epsom salt effectively reduces OA pain.[11]

Magnesium sulfate contained in Epsom salt can reduce pain and inflammation.[12,13] Many studies have examined magnesium and sulfate to reduce pain, especially in OA.[14,15] Previous studies have proven that magnesium in mineral supplements (Aquamin) can alleviate OA symptoms.[16] Combining magnesium and vitamin C can relieve synovitis,[17] and magnesium nutritional supplements can slow the progression of OA and relieve pain.[15]

Epsom salt has only been used using warm water by compressing, foot soaking, and bathing. However, such therapy requires a long preparation, so making a magnesium salt formula that is more practical, durable, and easy to use is necessary. Gel formula was chosen because it is easy to dry and wash and is durable. Therefore, this study aims to formulate Epsom salt gel and conduct clinical trials to test its effectiveness in reducing OA pain. This study hypothesizes that Epsom salt can be formulated into a gel, and the formula can reduce pain in OA patients.

MATERIALS AND METHODS

Design

This study is true-experimental with a Completely Randomized Design (CRD).[18]

Location

Preparation and formulation tests were conducted at the Pharmaceutical Technology Laboratory, Faculty of Pharmacy, Universitas Muhammadiyah Purwokerto. Meanwhile, the clinical trial stage was conducted in Linggasari Village, Kembaran District, Banyumas Regency, Central Java Province, Indonesia.

Formulation and testing stages

Tools and materials

The tools used include analytical scales, Beaker glass, Object glass, pH meter, diameter round glass, vernier, stirrer, porcelain cup, measuring cup, magnetic stirrer, gel container, cotton, hot plate, gloves, and centrifuge. The materials used in this study are Epsom salt, Na-CMC, Glycerin, Propylene glycol, and distilled water.

Preparation of Epsom salt gel formula

Epsom salt was scaled by its various concentrations (0.5 grams for 2% concentration; 0.625 grams for 2.5% concentration; and 0.75 grams for 3% concentration); each was dissolved into 2.5 grams of glycerin, heated and stir slowly, then was added with CMC-Na, 1.25 grams, and hot distilled water and stirred until it was fluffy. Then, it was added with propylene glycol (1.25) grams and hot distilled water and continuously stirred to disperse and form a gel ultimately.[19,20]

Physical properties testing

The gel was tested in several aspects, including organoleptic, homogeneity, consistency, pH, and spreadability. An organoleptic test is carried out to see the physical appearance of the formula by observing its shape, color, and smell. The homogeneity test is to determine whether it is homogeneous or not. The consistency test evaluates its stability by observing some changes in the formula after centrifugation. The pH test is to know its acidity level, ensuring it is safe for the skin. The spreadability test was conducted to ensure the even distribution of the gel when applied to the skin.[21]

Clinical test stage

Sample

Twenty-two respondents diagnosed with OA were included in this study; the sampling was randomized with inclusion criteria: male and female, their age >18 years, having OA pain, and willing to participate in the study until the end. OA surgery patients and respondents who did not complete the intervention were excluded from this study.[22]

Experimental procedures

There were five types of interventions, namely: A) pure gel administration intervention (negative control); B) Epsom salt gel with 2% concentration; C) Epsom salt gel with 2.5% concentration; D) Epsom salt gel with 3% concentration, and E) Diclofenac sodium (positive control). Each respondent received the five treatments randomly. There was a period between the first and the following treatment; the time lag was arranged based on the recurrence of OA pain in each corresponding respondent. The experimental procedure in this study can be seen in Table 1.

Table 1: Experimental procedure

Respondent	Treatment 1	Treatment 2	Treatment 3	Treatment 4	Treatment 5
1	A	B	C	D	E
2	E	A	B	C	D
3	B	C	D	E	A
n	…	…	...	…	…

Variable, instrument, and measurement

The variable assessed in this study is the pain scale. It was assessed at the beginning and the end of each treatment. The instrument used is the Numerical Rating Scale 11 (NRS-11).[23]

Statistical analysis

It used One-Way ANOVA and Tukey HSD statistical tests to determine the difference in mean pain levels between treatment groups.[24]

Ethical consideration

This research has received approval from the Health Research Ethics Commission of Muhammadiyah Purwokerto University with registration number: KEPK/UMP/38/XII/2021.

RESULTS

Epsom salt gel formulation and tests results

Figure 1 is the final result of the Epsom salt gel formula that has passed several physical and response tests (organoleptic, homogeneity, pH, spreadability, and consistency) (Table 2). The gel formula comprises Na-CMC, glycerin, propylene glycol, and active ingredients, namely Epsom salt containing magnesium sulfate.

(A) Concentrate of 2%

(B) Concentrate of 2.5%

(C) Concentrate of 3%

Figure 1. The formula of Epsom salt gel. A gel of Epsom salt with the concentration of 2% (A), 2.5% (B), and 3% (C)

Table 2 shows that the color produced by Epsom salt gel is clear white. It does not smell just like the gel base (odorless). All gel formulas are semisolid with different viscosity for each concentration variation (2%, 2.5%, and 3%). The higher the concentration of active substances, the more viscosity will increase. No coarse grain was identified based on the homogeneity test, meaning the Epsom salt gel formula is homogeneous. The PH test results show an average result of 6. Thus it meets the PH criteria safety for the skin at the interval of 4.5-6.5. The spreadability of the formula ranges from 4-4.53 cm (its mean is 4.36 cm); it is not good. The consistency test results proved that the gel did not separate. This means that the formula is physically stable for storage within a year.

Table 2: Organoleptic test, homogeneity, pH, spreadability, and consistency of the formula

Parameter	Negative Control	Concentration 2%	Concentration 2.5%	Concentration 3%	Positive Control
Organoleptic					
Color	Clear white	Clear white	Clear white	Clear white	Clear white
Odor	Odorless	Odorless	Odorless	Odorless	Odorless
Solidity	Semisolid	Semisolid	Semisolid	Viscous semisolid	Liquid semisolid
Homogeneity	Homogeneous	Homogeneous	Homogeneous	Homogeneous	Homogeneous
pH	6	6	6	6	6
Spreadability	4.63	4.53	4.2	4	5.8
Consistency	Consistent, no separation	Consistent, no separation	Consistent, no separation	Consistent, no separation	Consistent, no separation

The clinical test results

In this study, the characteristics of respondents were predominantly female (59%), with ages ranging from 45-59 (63.6%). All respondents experienced OA pain in their knees (100%) (Table 3).

Table 4 shows the lowest mean pain scale seen in the positive control group using diclofenac sodium (1.77+0.9), followed by the Epsom salt gel group with a concentration of 3% (2.68±0.9), the 2.5% group (3.64±0.9), the 2% group (4.18±1.0) and the control group (6.14±1.0). One-Way ANOVA statistical analysis showed a significant difference in OA pain between the treatment groups ($p<0.0001$).

Table 3: Characteristics of respondents (n=22)

Characteristic	Result
Sex	
Male	9 (40.9%
Female	13 (59%)
Age (yrs)	
<45	4 (18.8%)
45-59	14 (63.6%)
60-74	3 (13.6%)
75-90	1 (4.5%)
Spot of pain	
Knee	22 (100%)

Table 4: Analysis of differences in the mean of OA pain scale between groups

Group	Mean±SD	Mean square	F	P value
Negative control	6.14±1.0	60.068	65.981	0.000
Gel concentration of 2%	4.18±1.0			
Gel concentration of 2.5%	3.64±0.9			
Gel concentration of 3%	2.68±0.9			
Positive control	1.77±0.9			

One-Way ANOVA Test

Table 5 shows that all concentrations reduce OA pain levels ($p<0.0001$ vs. Negative control). The gel with a concentration of 3% has a higher effectiveness than others with lower concentrations, 2% and 2.5% ($p<0.0001$). A higher concentration of Epsom salt gel increases its effectiveness in reducing OA pain.

Table 5: Multiple comparison of OA pain reduction effectiveness between groups

Groups (I)	Groups (J)	Mean Difference (I-J)	*p-value*	95% CI	
				Lower	Upper
Negative control	Gel concentration of 2%	1.95455	0.000	1.1560	2.7531
	Gel concentration of 2.5%	2.50000	0.000	1.7015	3.2985
	Gel concentration of 3%	3.45455	0.000	2.6560	4.2531
	Positive control	4.36364	0.000	3.5651	5.1622
Gel concentration of 2%	Negative control	-1.95455	0.000	-2.7531	-1.1560
	Gel concentration of 2.5%	0.54545	0.326	-0.2531	1.3440
	Gel concentration of 3%	1.50000	0.000	0.7015	2.2985
	Positive control	2.40909	0.000	1.6105	3.2076
Gel concentration of 2.5%	Negative control	-2.50000	0.000	-3.2985	-1.7015
	Gel concentration of 2%	-0.54545	0.326	-1.3440	0.2531
	Gel concentration of 3%	0.95455	0.011	0.1560	1.7531
	Control positive	1.86364	0.000	1.0651	2.6622
Gel concentration of 3%	Negative control	-3.45455	0.000	-4.2531	-2.6622
	Gel concentration of 2%	-1.50000	0.000	-2.2985	-0.7015
	Gel concentration of 2.5%	-0.95455	0.011	-1.7531	-0.1560
	Control positive	0.90909	0.017	0.1105	1.7076
Positive control	Negative control	-4.36364	0.000	-5.1622	-3.5651
	Gel concentration of 2%	-2.40909	0.000	-3.2076	-1.6051
	Gel concentration of 2.5%	-1.86364	0.000	-2.6622	-1.0651
	Gel concentration of 3%	-0.90909	0.017	-1.7076	-0.1105

Tukey HSD Test

DISCUSSION

As hypothesized, this study has successfully formulated Epsom salt-based gel with three variants, namely 2%, 2.5%, and 3% concentration. All of them have met the physical properties test standards of the formula, as shown in Table 2. Testing on organoleptic parameters has obtained maximum results where all the formulas were semisolid with varying viscosity for each concentration (higher concentration of the active substance makes it thicker), clear gel, and odorless.

Based on the homogeneity test, the formulation results are homogeneous. It was carried out as follows: the gel was applied to a transparent glass, then observed thoroughly from the top, middle, and bottom. The absence of coarse grains indicates homogeneity. The active substance will only be distributed entirely if the formula is homogeneous.[25] The pH test is carried out to see the acidity of the gel to ensure that it will not cause any irritation to the skin. The gel was measured using a universal pH stick. The pH test results showed that the gel met the skin pH criteria (4.5-6.5).[26,27]

The formula only failed on its spreadability parameter (a mean of 4.36 cm); this means that it needs not better spreadability. A good spreadability of the gel formula is 5-7 cm. The test is carried out to ensure an even distribution of the gel as it is applied to the skin. A good spreadability means a good distribution of active ingredients on the skin; in turn, its beneficial effect will cover more area. The gel spreadability is affected by its viscosity. A thicker viscosity will negatively affect its spreadability. The study proved that all gel formulas with a higher concentration of Epsom salt have low spreadability.[28,29]

The consistency test results show that all gel formulas did not show any separation after centrifugation. This indicates that they remain stable and are not affected by gravitational forces for year storage. The Epsom salt gel formula does not contain any preservatives, so it has the potential to grow mold at room temperature in a week. It can stay without mold for two months by putting it in the fridge.[30,31]

Clinical trials on 22 respondents with OA pain have proved that all Epsom salt gel concentrations have effectively reduced pain. Its highest variant is more effective in reducing OA pain than the others. It has almost the same effectiveness as diclofenac sodium. The working mechanism of magnesium in relieving OA pain inhibits the entry of Potassium ions (K^+) into cells. Cells with an injury (inflammation) will release chemical mediators of pain, including prostaglandins, H^+ ions, and intracellular K^+, which act as primary activators of

nociceptors. Nociceptors convert the stimulus into impulses that will be flowed and processed in the central nervous system, which is then perceived as pain. Magnesium blocks NMDA receptors, an ion channel receptor (one of which is the K+ ion), so that nociceptors are not activated, and pain impulses do not reach the central nervous system.[13,32]

The results of this study support previous research, which concludes that Epsom salt effectively reduces knee pain in the elderly suffering from OA.[33] A similar study has also proved that administering magnesium oil can reduce inflammation and pain and induce joint repair in people with arthritis.[34] Another study has also shown that using salt water baths in the dead sea with much magnesium can improve the daily activities of people with rheumatoid arthritis and reduce the complaints due to the disease.[35] People with OA tend to experience magnesium deficiency. Magnesium's absorption through the skin helps satisfy the body's minerals and reduces inflammation.[36] In addition, another research also claims that bathing with magnesium salt solution can reduce stress.[37]

Apart from being used for bathing (Balneotherapy), there are various ways to use magnesium salts in OA sufferers as a complementary therapy, including for dietary use; one study found dietary magnesium could potentially prevent OA because magnesium deficiency can cause delays in cartilage and bone differentiation leading to OA.[15,38] Another study also found that intra-articular administration of magnesium and vitamin C can reduce joint damage and pain in OA.[17] The results of this study provide a new alternative for using magnesium sulfate as a therapy for OA sufferers, namely by using it topically, which is more practical.

CONCLUSION

Epsom salt can be formulated into gels with different concentrations. All concentrations of Epsom salt gel are effective in reducing OA pain levels; however, the higher the concentration of Epsom salt gel, the more effective it is in reducing OA pain.

ACKNOWLEDGMENTS

Universitas Muhammadiyah Purwokerto for funding

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