



Formulation and Evaluation of Patch Preparations for Respiratory Relief from a Blend of Extracts and Essential Oils of Ginger Rhizome

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Article Info:

Abstract



Article History:

Received 23 May 2022
Reviewed 30 June 2022
Accepted 09 July 2022
Published 15 July 2022

Cite this article as:

Astuti RD, Simamora S, Tedi, Taswin M, Formulation and Evaluation of Patch Preparations for Respiratory Relief from a Blend of Extracts and Essential Oils of Ginger Rhizome, Journal of Drug Delivery and Therapeutics. 2022; 12(4):64-67

DOI: <http://dx.doi.org/10.22270/jddt.v12i4.5448>

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Ginger (*Zingiber officinale* Rosc.) - a plant from the Zingiberaceae family containing 2-3% essential oil- has proven to have a good effect on loosening the chest cavity. In this study, pharmaceutical preparations for respiratory tablets in the form of patches have been developed, which are used by placing them on the skin, clothes or masks associated with the user. A patch formula containing a mixture of 3% ginger extract and ginger essential oil was created at 0.1%, 0.2% and 0.3%, respectively, with variations of PVA and PVP as polymers to control the release of ginger essential oil as a breathing reliever. Each preparation with ginger essential oil content used PVA and PVP with variations of 1:1, 1:1.5 and 1:2. The practices were evaluated for 21 days on days 0, 7, 14, and 21. The evaluations carried out were pH, weight uniformity, patch thickness, folding resistance, color and odor changes, moisture content and organoleptic tests. After obtaining long-lasting results, an irritation test was carried out on the respondents. The results showed that during storage for 21 days, the pH was in the range of 5.14-6.11, weight uniformity ranged from 1.24 g-1.65 g, humidity 7.18%-8.88%, and folding endurance >300 times. The variation of PVA and PVP shows that the higher the PVP content, the weight of the patch increases and the humidity decreases. So it can be concluded that a good formula is a formula with variations of PVA and PVP 1: 1.5 and ginger essential oil content of 0.3%. After obtaining long-lasting results, an irritation test was carried out on the respondents. The results showed that during storage for 21 days, the pH was in the range of 5.14-6.11, weight uniformity ranged from 1.24 g-1.65 g, humidity 7.18%-8.88%, and folding endurance >300 times. These alterations, do not change color and odor nor irritate the respiratory tract. The variation of PVA and PVP shows that the higher the PVP content, the weight of the patch increases, and the humidity decreases. So it can be concluded that a good formula is a formula with variations of PVA and PVP 1: 1.5 and ginger essential oil content of 0.3%; the weight of the patch increases, and the humidity decreases. So it can be concluded that a good formula is a formula with variations of PVA and PVP 1: 1.5 and ginger essential oil content of 0.3%.

Keywords: ginger essential oil, respiratory lozenges, patch, PVA, PVP

INTRODUCTION

Ginger (*Zingiber officinale* Rosc.) is a plant from the Zingiberaceae family, which is widely used as traditional medicine in various countries. In China, ginger reduces nausea, gastritis and gastric ulcers, abdominal pain, diarrhoea, coughs, and rheumatism. In India, ginger is also used to reduce nausea, treat asthma cough, reduce severe and sudden pain, overcome heart palpitations, treat digestive disorders, and treat rheumatism. Most Europeans also consume ginger tea to treat indigestion.

The part used is the rhizome which contains 2-3% essential oil. The chemical constituents are zingiberene, cineol, limonene, geraniol, citral, eucalyptol and camphor. The ginger essential oil has been used traditionally to treat various problems in the respiratory tract. It has been scientifically proven by several studies showing the effect of loosening the chest cavity. Therefore, in this study, a pharmaceutical preparation for respiratory lozenges in the form of a patch will be developed (Mao et al., 2019).

The patch is a medicinal preparation in the form of an adhesive to be placed on the skin, has different sizes and is maintained for an extended time. Patches can be used by

affixed to the skin, clothes or other materials related to the user. Patch preparations circulating in the market are nicotine patches, wound plasters, and transdermal patches. This research will develop a patch preparation containing ginger oil for respiratory tablets that can be used for children and adults.

Patch-forming materials are polymers such as PVP (Polyvinylpyrrolidone) and PVA (Polyvinyl alcohol), which are types of synthetic polymers that can produce thin and flexible preparations because the nature of the substance makes it easier to adjust the shape and content (Journal et al., 2016). In addition, applying polymers from patch preparations is a substance to control drug release and can be used to formulate various controlled drug delivery systems. This is very useful for releasing active substances in the form of oil to help relieve breathing.

According to Fatmasari (2017), who researched patch preparations, NaF, PVA and PVP have the best combination in a 2:1 ratio compared to others, namely 1:1 and 1:2. This is the basis of this research to make a patch containing a mixture of ginger extract with various concentrations of ginger oil by varying PVA and PVP and test its effectiveness as a respiratory lozenge.

RESEARCH METHODS

This research is an experimental study on the formulation and tests the effectiveness of ginger rhizome essential oil (*Zingiber officinale Rosc.*) In the formulation of patch preparations for respiratory lozenges

Tools and materials used include measuring cups, gram scales, gram weights, glass stirrer, analytical balance, wood tongs, water bath, watch glass, pH meter, desiccator, screw micrometer, ruler, questionnaire, parchment paper, peak flow meter, ginger extract, ginger rhizome essential oil (*Zingiber officinale Rosc.*), Polyvinylpyrrolidone (PVP),

Polyvinyl Alcohol (PVA), Polyethyleneglycol 400 (PEG400), Tween 80, Span 80, Nipagin, Aquadest, Silica Gel, and Ethanol. In this study, the formula used refers to Akuba's study (2019), which tested the effectiveness of the repellent patch against mosquito bites by using a combination of PVA and PVP polymer ratios of 1:1. In another study, Fatmasari (2017) tested the physical stability of the patch with a mixture of PVA and PVP polymers with the best ratio of 2:1. So in this study, variations of PVA and PVP of 1:1, 1:1.5 and 1:2 will be carried out. The content of a ginger extract is 3%, and the oil essential of ginger rhizome used were 0.1%, 0.2% and 0.3%. Thus, there are 9 formulas.

Table 1: Patch Formula Containing a Mixture of Extracts and Essential Oils

Ginger Rhizome with PVA and PVP Variations

No	Ingredient	Amount of Ingredients per Formula									Note:
		F1	F2	F3	F4	F5	F6	F7	F8	F9	
1	Ginger Extract	3%	3%	3%	3%	3%	3%	3%	3%	3%	Active substance
2	Ginger Oil	0.1%	0.2%	0.3%	0.1%	0.2%	0.3%	0.1%	0.2%	0.3%	Active substance
3	PVA	7%	7%	7%	7%	7%	7%	7%	7%	7%	Polymer
4	PVP	7%	7%	7%	10.5%	10.5%	10.5%	14%	14%	14%	Polymer
5	PEG 400	13%	13%	13%	13%	13%	13%	13%	13%	13%	Plasticizer
6	nipagin	0.01%	0.01%	0.01%	0.01%	0.01%	0.01%	0.01%	0.01%	0.01%	Preservative
7	A mix of Tween 80 and Span 80	1%	1%	1%	1%	1%	1%	1%	1%	1%	Emulsifier
8	Water up to	100	100	100	100	100	100	100	100	100	Solvent

PVA: Polyvinyl alcohol, PVP: Polyvinyl pyrrolidone, PEG 400: Polyethylene glycol

PVA was developed in 100 ° C hot water to form a gel mass, and then PEG 400 and a mixture of PVP K30 and Nipagin in 96% ethanol were put into the gel mass.

Tween 80 and span 80 were mixed with ginger extract and essential oil, stirring with the gel mass first and adding the remaining water. When homogeneous, they were poured into the mold, and dried at room temperature for 2x24 hours. After drying, the patch was cut with a size of 2x4 cm² and then stucked on the hypafix plaster with a size of 5x3 cm

Evaluations on this patch preparation were physical stability, organoleptic, and irritation tests on 30 respondents.

Observations were made on days 0, 7, 14 and 21. Physical stability tests include pH, weight uniformity, patch thickness, folding endurance, moisture content test, and organoleptic (color, shape and odor).

The respondents were adolescents aged 18 years, in good health, had no history of diseases related to the respiratory tract and allergies were unmarried and willing to sign the consent form.

RESULTS

Physical Stability Test

Table 2: Physical Stability Test Results of Patch Preparations Containing a Mixture of Ginger Rhizome Extract and Essential Oil for 21 Days

No.	Stability Test Type	Average Observation Results per Formula								
		F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Weight (g)	1.24±0.08	1.24±0.07	1.24±0.04	1.30±0.01	1.30±0.07	1.31±0.06	1.41±0.07	1.41±0.06	1.43±0.03
2	pH	5.32±0.06	5.31±0.07	5.35±0.07	5.34±0.05	5.33±0.05	5.35±0.08	5.30±0.07	5.32±0.03	5.32±0.06
3	Folding Durability	>300	>300	>300	>300	>300	>300	>300	>300	>300
4	Humidity (%)	8.63±0.01	8.65±0.01	8.65±0.02	7.93±0.01	7.68±0.01	7.45±0.03	6.88±0.02	6.48±0.02	6.35±0.02
5	Thickness(mm)	0.54±0.03	0.55±0.02	0.54±0.02	0.55±0.02	0.55±0.02	0.55±0.03	0.55±0.02	0.55±0.02	0.55±0.01

Organoleptic Test

Table 3: Results of Organoleptic Test on Patch Preparations Containing a Mixture of Ginger Rhizome Extract and Essential Oil by 30 Respondents after 21 Days of Storage

No.	Types of Organoleptic Test	Formula								
		F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Homogeneity	H	H	H	H	H	H	H	H	H
2	Color	TB (100%)	TB (96.7%)	TB (96.7%)	TB (96.7%)	TB (96.7%)	TB (100%)	TB (100%)	TB (100%)	TB (100%)
3	Smell	TB (90.0%)	TB (90.0%)	TB (90.0%)	TB (96.7%)	TB (96.7%)	TB (100%)	TB (96.7%)	TB (97.7%)	TB (100%)

H : Homogeneous, TB : Unchanged

Irritation Test

The irritation test was carried out on 30 respondents who had signed the consent form using formula 6 containing PVA and

PVP in a ratio of 1: 1.5 and ginger rhizome essential oil as much as 0.3%. The test was carried out by attaching a patch to the mask and used by the respondent for 30 minutes.

Table 4: Irritation Test Results for Patch Preparations Containing a Mixture of Extracts and Oils Essential Ginger rhizome to 30 respondents

No.	Observation Type	Observation result	
		Yes	Not
1.	Pain in the Nose	0	30 people
2.	Nose becomes stuffy	0	30 people
3.	Hot feeling in the nose	0	30 people

DISCUSSION

Weight Uniformity

This test was conducted to determine the uniformity of the weight of each patch. In this study, the weight per patch was not planned because each formula has a different concentration of the active substance and PVP. This test was carried out by weighing the weights of 5 randomly selected patches from each formula at the time of observation, namely the 0, 7th, 14th and 21st days after storage, then calculated the average weight and standard deviation of the measurement results (Sharma et al., 2013)

The results showed that the weight of the patch for each formula with the same size and volume, increased with increasing levels of PVP. The highest weights were seen in F7, F8 and F9, which contained PVP with a group of 14%. This shows that PVP can increase the weight of the patch (Rowe, Sheskey and Quinn, 2009).

pH

The test was carried out by developing 1 patch in 2 ml of water for each formula at each observation time of days 0, 7, 14 and 21 after storage. The patch was allowed to swell for 2 hours and the pH was checked using a pH meter.

The results indicate that this patch preparation of ginger rhizome extract and essential oil mixture for each formula has an average pH of around 5.3 which is still in the 4-8 range. The pH of ginger extract and essential oil was around 6, but the pH of PVP was in the acidic range. This causes the pH of the patch to be 5.3.

Folding Durability

Fold resistance is the number of folds required to break the patch. This test describes the strength of the polymer's patch and how efficiently the polymer and plasticizer provide flexibility. In this case, the polymer is a combination of PVA and PVP, and the plasticizer is PEG 400. The test method is to fold the patch repeatedly in the same place until damage occurs. A patch is said to meet the criteria if it is resistant to folds more than 300 times (Lakhani et al., 2015)

In the study of folding endurance, all patch formulas met the requirements because >300 times of folding did not experience damage. This shows that polymers and plasticizers can provide optimal flexibility in this patch preparation containing a mixture of extracts and essential oils of ginger.

Percent Humidity

The moisture percentage test aims to determine the moisture content in the patch preparation, which can affect the stability of the trial. Water content that is too high will facilitate the occurrence of microorganism contamination so that the strength of the preparation will be reduced (Shivaraj et al., 2010). This test was carried out by inserting the patch into a desiccator containing silica gel for 24 hours and the initial weight and weight after storage was calculated. The test was repeated 3 times for each formula and at each observation time, namely the 0, 7, 14 and 21 days after storage, then the average percent humidity and standard deviation were calculated.

Percentage of patch moisture for each formula decreased with increasing PVP levels. In this patch preparation, a

mixture of PVA and PVP is used as a patch-forming polymer. PVA is a polymer that easily binds to mucus or liquids. So it is often used in mucoadhesive preparations such as buccal patches. The interaction of PVA with PVP can decrease the mobility and flexibility of PVA to fluids.

For this reason, a patch containing a mixture of PVA and PVP with a higher concentration of PVP will reduce the tendency of the patch to bind to fluid or moisture (Jaipakdee, Pongjanyakul and Limpongsa, 2017). This causes a decrease in humidity with increasing levels of PVP.

Thickness

Tests for patch thickness are carried out to see the uniformity of the thickness of the resulting patch. The thickness obtained indicates the uniformity of the volume of the patch solution that is poured into the mold. This test is carried out by measuring the patch at three different points using a micrometer screw. Then the average thickness and standard deviation were calculated to ensure the same thickness in each patch (Lakhani et al., 2015). The test was carried out 3 times on each formula

The results showed that the relative patch thickness did not differ for each formula. However, after 21 days of storage, the thickness of the patch decreased slightly due to evaporation of the water content in the patch.

Organoleptic

Respondents observed changes in the preparations aged 0, 7, 14 and 21 days. The parts observed were homogeneity, odor changes and color changes after being stored for 21 days. The results showed that there was no change in inhomogeneity. The preparations were still in a homogeneous state.

The preparations stated by all respondents did not change for changes in odour were F7 and F9. As for color, the preparations that were declared unchanged were F1, F6, F7, F8 and F9

Irritation Test

The test was carried out on 30 respondents who had met the inclusion criteria and signed a letter of approval by attaching a patch to the mask and using the respondent for 30 minutes. Respondents may stop testing if it occurs pain in the nose, feeling stuffy nose and shortness of breath or burning sensation when breathing.

From the results of observations and filling out questionnaires by respondents, there were no signs of irritation in the respiratory tract, and the 30 respondents said "no" for the three characteristics of irritation so that the preparation is declared not to irritate the nasal mucosa.

This is the basis for further research to test the effectiveness of a mixture of ginger extract and essential oil as a respiratory patch. Because ginger and its bioactive compounds such as 6-gingerol, 8-gingerol, 6-shogaol, citral and eucalyptol can relax airway smooth muscles and reduce airway resistance (Mao et al., 2019)

CONCLUSION

After formulation and evaluation of physical, organoleptic and respiratory tract irritation on patch preparations containing a mixture of extracts and essential oils of ginger, it can be concluded that the most physically stable formula, does not undergo organoleptic changes and is not irritating to

the respiratory tract is the formula containing essential oils. ginger essential 0.3% with PVP content of 10.5%.

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