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Research Article

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FORMULATION AND EVALUATION OF HYDROGEL CONTAINING TAGETES ERECTA L. LEAVES ETANOLIC EXTRACT

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Abstract

Hydrogel is quite convenient dosage used in topical therapy. The ethanol extract of Tagetes erecta L. leaves can be used as the active ingredient of hydrogel. The combination of base carbopol, gelatine and Na-CMC can be applied in the manufacturing process.Getting hydrogel with the active ingredient content of extract of T. erecta leaves that have physical properties and good physical stability based on the expected parameters.

Hydrogel base are Carbopol, Gelatine, Na-CMC with the other ingredients are ethanol, propylene glycol, triethanolamine and distilled water. Physical properties tested were organoleptic, pH, spreadability and viscosity. Physical stability testing for 90 days at a temperature of 45°C with 75% RH values using a tool climatic chamber, physical properties testing performed on days 30, 60, and 90th. The resulting hydrogel perfomed on days 0 has good physical properties and the corresponding expected parameters. The resulting physical stability in accelerated stability testing for three months only 5th formula also corresponds the parameters required.

Key Words: Hydrogels, Tagetes erecta l., Hydrogel Base, Physical Properties.

INTRODUCTION

Indonesia is a vast country with a tropical climate and fertile land.This situation led to many plants thrive, including medicinal plants.Indonesia has a lot of medicinal plants and easily found around us because the plants thrives.Indonesian society have long used plants in traditional medication.The use of medicinal plants are increasingly popular and increasingly expanding globally with the development of science.

Tagetes erecta. L is a medicinal plant that thrives in Indonesia.T.*erecta* or American merigold is the *Asteraceae* family with Indonesian name *kenikir liar* or *bunga tahi kotok* (Hembing, 2000; Priyanka et al., 2013). Chemical constituents contained in the plant T. *erecta*are saponins, flavonoids, terthienil, helenial, and flavoxanthin (Gong et al., 2012; Jain et al., 2012). This plant is antiseptic and larvacide that can kill microorganisms including bacteria, fungi, and larva. T. *erecta* traditionally treat diseases caused by microorganisms such as eye infection, urinary tract infection, bronchitis, heal ulcers, and inflammation (Jain et al., 2012; Tahir and Khan, 2012). The ethanol extract of T. *erecta* leaves in a variety of studies have been reported to be beneficial in the healing process.Water-alcohol extract of leaves of T. *erecta* has been tested able to heal the wounds of mouse skin and its ability to heal wounds better than water-alcohol extract of *Centella asiatica* leaves (Chatterjee et al., 2011). The ethanol extract of T. *erecta* with a dose of 100mg/kg are also reported to be able to protect the kidneys of test mice from acid irritation properties thiobarbiturate (Nishanthi and Anuradha, 2012).

The 10 mg/ml ethanol extract of T. *erecta*leaves has antibacterial against *Bacillus subtilis, Staphylococous aureus, Echerichai coli, Staphylococous lutea,* and *Bacillus circulence* (Verma and Verma, 2012).

Based on the benefits ethanol extract of T. *erecta* leaves it needs to be developed into a pharmaceutical dosage form.Development of pharmaceutical formulations with an active ingredient extract of T. *erecta* is expected to guarantee the safety, effectiveness, and convenience for patients who use it. Hydrogel is one of the pharmaceutical dosage forms are convenient when used in wound healing therapy. Hydrogels can create moist conditions in the wound area which will accelerate the wound healing process. Hydrogels also provides cool effects that can help eliminate the red color of the skin and swelling that occurs. Hydrogels with physical properties will be able to reduce the pain and also improve the comfort of patients who use it (Das et al., 2011; Leelapornpisid et al., 2014; Okan et al., 2007).

Hydrogel base is a critical factor to produce preparations having good physical properties and assist the process of wound healing in patients. Carbopol 940 is used as the base hydrogel in the amount of 0.5 to 2.0%.Na-CMC as a base will make a softer gel is usually used in the amount of 3.0 to 6.0%. Gelatine as a base to use a minimum amount of 0.5% will be able to improve the absorption properties of the preparation (Garg et al., 2002).

Based on these descriptions have never found a study of the composition of the three bases that are formulated in the form of a hydrogel with an active ingredient ethanolic extract of T. *erecta*.

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The aim of this study was to utilize the T. *erecta* leaves to formulate in pharmaceutical dosage forms easier to use by people.The second objective was to determine the physical properties and stability of hydrogel preparations produced from a mixture of Carbopol, Na-CMC, and Gelatine.

Experimental

MATERIALS AND METHODS

Plant materials

T. erecta leaves collected from the plantation farmers from Bandungan, Ambarawa, Central Java. Leaves collected from plants that lived about 3 to 4 months, or just before flowering. The collected leaves were authenticated by Pharmaceutical Biology Department, Faculty of Pharmacy,University of Gadjah Mada, Indonesia.

Chemicals

Carbopol 940 (Fagron), NA-Carboxy Methyl Cellulose (Dai-Ichi), Gelatine (Gelita), Propylene glycol (Dow Chemical Co), Triethanolamine (Merck), Glycerol (P&G), and Ethanol.

Preparation of extract

The powdered *T. erecta* leaves were used for extraction using maseration method. The powdered were loaded in beakerglass and extracted with 96% ethanol, stirred at a speed of 200 rpm for 24 hours. Finally the extracts ware filtered and concentrated using vacuum rotary evaporator. Concentrated extract was stored at 4-8°C until used.

Formulation of gels

Hydrogel made seven formulas and all formulas containing Carbopol 940, Gelatine and Na-CMC as a base with a few variations of weight, modification from Edy et al., (2016). Other content of the hydrogel formulation are viscous ethanol extract of leaves*T. Erecta*, propylene glycol, tri-ethanolamine, ethanol, glycerol, and distilled water in a quantity sufficient to prepare 100 g of hydrogel. Distilled water was divided in to four parts. Carbopol 940 was dispersed in first part of water, gelatin was dispersed in second part of water, and Na-CMC was dispersed in third part of water for 24 hours. 2.5 g viscous extract was dissolved in ethanol.

After 24 hours, Carbopol 940, Gelatine and Na-CMC which has been expanding stirred using a hand mixer until homogeneous. Propylene glycol and glycerol were added to the mixture under continuous stirring. Tri-ethanolamine was added drop wise to the mixture for adjusment of required skin pH (6.5-7) under continuous stirring. The mixture was viscous leaf extract of T. *erecta* in ethanol included in the base slowly while still stirring until homogeneous. Hidrogel volume made up to 100 g by adding remaining distilled water under continuous stirring. Composition of hidrogel formulation is given in Tabel 1.

Evaluation of Hidrogel Formulation

Physical Evaluation and Subjective Properties – The colour, appearance, feel on aplication, consistency, and texture were personally noted and by personal observation.

pH – The pH of hidrogel formulation was determined by using a digital pH meter (Oakton-eutech instruments).

Viscosity – The measurement of viscosity of hidrogel by using viscometer (Rion viscotester VT-04F) with spindel no. 2. Hidrogel was taken in a beaker until full and the spindel was dipped in it about 2 minutes and then the reading was taken.

Spreadability – Two sets of circular glass plates (diameter 15 cm) were taken. The hidrogel (1 g) was placed over one of plates and the other plates was on the top of the hidrogel. The standart weight applied on the upper plates was 125 g weighted for 1 minutes. The spreadability of the hidrogel was determined by measuring the area of circle spreading formed.

Stability study

The stability study was performed at climatic chamber (memmert). Formulated hidrogel preparation at condition of accelerated stability testing (temperature 45°C ± 2°C and humidity 75% ± 5% RH) for three monts. The following parameters of the hidrogel such as physical evaluation and subjective properties, ph, viscosity, spreadability were studied every 30 days.

RESULT AND DISCUSSION

Hydrogel is made in a sterile room with a mixture of bases are Carbopol 940, Gelatine and Na-CMC.

Table1 Composition of T. *erecta* hydrogels modification of Edy et al., (2016)

Formulation	Carbopol 940 (%)	Gelatine (%)	NA-CMC (%)	Propylene glycol (%)	Tri etanolamin (%)	Glycerol (%)	Extract (%)	Etanol (%)	Distilled water (%)
F1	1,25	0,3	0,2	2	3	12,5	2,5	5	Up to 100
F2	0,75	0,8	0,2	2	3	12,5	2,5	5	Up to 100
F3	0,75	0,3	0,7	2	3	12,5	2,5	5	Up to 100
F4	1	0,55	0,2	2	3	12,5	2,5	5	Up to 100
F5	0,75	0,55	0,45	2	3	12,5	2,5	5	Up to 100
F6	1	0,3	0,45	2	3	12,5	2,5	5	Up to 100
F7	0,9	0,47	0,38	2	3	12,5	2,5	5	Up to 100

Hydrogel is then observed physically, hydrogel base are transparent white and then turns green light for the addition of extract of T. *erecta*. Hydrogel have a good consistency,smooth texture, and soft when applied to the skin.The physical appearance of the hydrogel can be seen in figure 1.

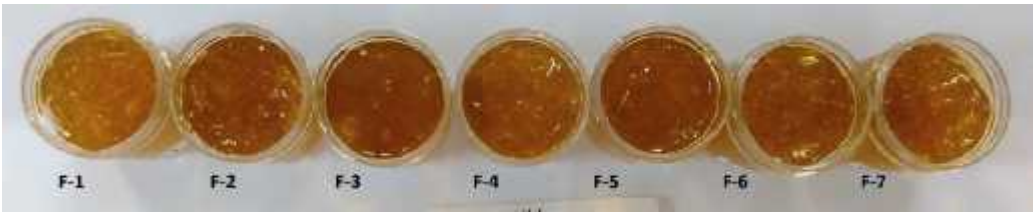

Fig 1 Pharmaceutical hydrogel containing *Tagetes erecta* L. leaves etanolic extract

Characteristics hydrogel at the time of manufacture or H-0 are pH, viscosity, and spreadibility. The same test was repeated on day 30, 60, and 90 after the hydrogel is stored in the climatic chamber withtemperature 45°C ± 2°C and humidity 75% ± 5% RH. All data about the physical characteristics and during stability testing presented in Table 2.

Table2 Characteristics of T. *erecta* hydrogels at Day 0, 30, 60, and 90

Formulation	pH				Spreadability (cm²)				Viscosity (dPa.s)			
Day	0	30	60	90	0	30	60	90	0	30	60	90
F1	6,48	6,45	6,50	6,47	11,34	14,51	15,90	19,63	300	290	275	200
F2	6,62	6,64	6,60	6,60	20,42	22,05	24,62	28,26	210	200	175	150
F3	6,71	6,70	6,70	6,68	29,21	32,15	36,3	40,69	140	125	100	50
F4	6,73	6,75	6,70	6,71	18,09	20,42	22,05	26,41	240	225	200	150
F5	6,75	6,70	6,72	6,69	30,18	31,16	34,19	38,46	140	130	100	50
F6	6,72	6,68	6,71	6,70	19,63	21,23	22,05	24,62	225	210	200	175
F7	6,55	6,50	6,52	6,53	16,61	18,09	19,63	23,75	250	240	210	175

The first test is to measure the pH value using a pH meter. At H-0 whole formula hydrogel have a pH value of 6.55 to 6.75, and meet the requirements of the pH value. During the test the stability of the entire formula hydrogel still has a pH value as required.The pH value of the hydrogel which is convenient when used is 6.2 to 7.2 and will not irritate the skin when used (Haneefa et al., 2010).

Viscosity on day 0 only 3th formula with a value of 140 d.PaS and the 5th formula with a value of 140 d.PaSmeet the requirements.Good value for the hydrogel viscosity is 50 to 150 d.PaS (Yuliani, 2012). Hydrogel with viscosity values above requirements will feel uncomfortable when applied to the skin. Hydrogel with viscosity grades lower than the requirements will be easily lost from the skin, thereby reducing the effects of treatment (Yuliani, 2005). After testing the stability for 90 days, The 3th and 5th formulas also still meet the requirements of viscosity value with a score of 50 d.PaS.

Standard spreadability for hydrogel is with diameter of 5–7cm or has spacious 19.50 - 38,50cm2 (Garg et al., 2002). H-0 are four formulas that meet the quality standards of the spreadability are 2nd formula with 20.42 cm², 3th formula with 29.42 cm², 5th formula with 30.18 cm², and the 6th formula with 19.63 cm². 1st, 2nd, and 7th formula have the value of the spreadabilityare smaller than the standard or less than 19.50 cm². After testing the stability of the only 2nd, 5th,and 6th formula are still meets the quality sandart spreadability.

CONCLUSION

The 5Th formula with a mixture of basis are Carbopol 940 weight of 0.75 g, 0.55 g Gelatine, and 0.45 g CMC is a formula that meets the quality parameters of the hydrogel.

On day 0 the 5Th formula have a pH value of 6.75, viscosity of 140 d.PaS, and the value of the spreadibility 30.18 cm². After testing the stability for 90 days, the 5Th formulation still meeting the quality parameters of hydrogel with a pH value of 6.69, a viscosity of 50 d.PaS, and the spreadibility of 38.46 cm².

Ethanol extract of T. *erecta* leaves weighing 2.5 g can be made into a good hydrogel with a base mixture of Carbopol 940 weighing 0.75g, Gelatine Na-CMC 0.55g, and 0,45g. This formula also has good physical performances so convenient to use in healing therapy. The extract of T. *erecta* leaves contained in the hydrogel also has good stability during storage so as not to damage hydrogel formed.

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