FORMULATION OF GEL FROM GYNURA SEGETUM EXTRACT AND ITS ACTIVITY ON BURN WOUND HEALING

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ABSTRACT
Objective: The aims of this study were to formulate gel from Gynura segetum (GS) extract and evaluate its burn-healing activity.

Methods: GS extract was formulated using carbomer and carboxymethylcellulose (CMC) as a stabilizer with various concentrations. Furthermore, the gel of GS extract was evaluated, including organoleptic, pH and viscosity. A burn-healing evaluation was conducted by making a wound with a hot plate on male Wistar rats, and 600 mg of the gel was applied. Subsequently, the presence of erythema and width contraction of the burns were observed for 15 d.

Results: The result showed that the formulation containing 1 % of carbomer and 1.2 % of GS extract has the best physical stability. The gel also increased the rate of the healing process with decreased burn wound contraction (5.67 mm after 15 d) and the erythema than the control (8.50 mm after 15 d). The significance value was less than 0.05, indicating that the rate of the healing process was significantly different between the GS extract gel and the control.

Conclusion: This finding demonstrated that the gel of GS extract can significantly improve the burns wound healing process and may also be safely used for topical preparation.

Keywords: Gynura segetum, Gel, Burn wound healing, Carbomer

Burn wound is a major health problem due to its incidence of serious complications [1], and it causes infections which have led to 50-75 % of hospital deaths [2]. The infection can also exacerbate systemic inflammation and delay re-epithelialization due to hypermetabolism and inflammation [3, 4] since many synthetic drugs have been used for wound healing. However, due to the occurrence of allergy and resistance [5], natural drugs are used as alternative.

Wound healing is the repair process following an injury to the skin or other tissues. Thereafter, an inflammatory response occurs to increase the collagen production by the cells below the dermis and the regeneration of epithelial tissue in the outer skin layer. The process is divided into three steps: inflammation, proliferation, and remodeling [6]. The ultimate goal of burn management is to heal wounds in a short time and prevent infection [7].

Gynura segetum (GS), family Compositae (Asteraceae) is a traditional plant found in the tropical regions of Indonesia and Malaysia [8]. It has been shown to treat cancer, diabetes, inflammation, hypertension, and skin afflictions [9]. Furthermore, the saponin and flavonoid contained in this plant act as anti-inflammation, analgesic, and antiseptic. Therefore, this study aimed to formulate gel from GS extract to increase the burn wound-healing process, and the activity, as well as the physical stability on storage, were also investigated.

The phytochemical screening of GS extract was conducted to detect secondary metabolites such as flavonoids, alkaloids, steroids, saponins, terpenoids and tannins [10].

| Materials         | Formula (%) |
|-------------------|-------------|
|                   | I  | II | III | IV | V  | VI |
| Carbomer          | 1  | 1.5| 2   | -  | -  | -  |
| CMC               | -  | -  | -   | 2  | 3  | 4  |
| Gynura segetum GS | 1.2| 1.2| 1.2 | 1.2| 1.2| 1.2|
| Propylene glycol  | 10 | 10 | 10  | 10 | 10 | 10 |
| Triethanolamine   | q.s| q.s| q.s | -  | -  | -  |
| Propylparaben     | 0.02| 0.02| 0.02| 0.02| 0.02| 0.02|
| Methylparaben     | 0.18|0.18 | 0.18| 0.18| 0.18| 0.18|
| Sodium EDTA       | 0.05|0.05 | 0.05| 0.05| 0.05| 0.05|
| Sodium Metabisulfite | 0.1| 0.1 | 0.1 | 0.1 | 0.1 | 0.1|
| Water add         | 100 | 100 | 100 | 100 | 100 | 100|

The gel formulation from the GS extract was prepared according to the formula shown in Table 1. Propylene glycol was admixed with water, and then carbomer and carboxymethylcellulose (CMC) were dispersed into the mixture of glycerine and distilled water, respectively. In addition, GS extract and other components were dissolved in the water and added into the obtained mixture. Triethanolamine (TEA) was also...
added and stirred until homogeneous mass of gel was formed [11]. The physical stability of GS extract gel was evaluated, including organoleptic, pH and viscosity [12].

The ethical approval for the experimental procedure was obtained from the Health Research Ethics Committee, Universitas Padjadjaran with No: 1291/LN6. C1.3.2/KEPK/PN/2016. The Male Wistar rats obtained from Lembang, West Java, Indonesia, were acclimated to laboratories conditions for 7 d. The Male Wistar rats were anesthetized by urethane, the hairs were shaved and the underlying skin was cleaned with ethanol. A metal cylinder (diameter 1 cm) heated in the water (80 °C) for 1 m was used to create the burns. The metal cylinder was exposed on the shaved area of the rats for 10 s. After the treatment, the burn-healing process was evaluated by measuring wound contraction and the presence of erythema [13, 14]. The wound surface area was traced on a transparent paper and calculated by the following equation:

\[
\% \text{ of wound contraction} = \frac{100 (A_o - A_t)}{A_o}
\]

Where \( A_o \) is the initial wound and \( A_t \) is the wound on t day.

These results were analyzed using the one-way analysis of variance (ANOVA) at the level of (P<0.05) and all data were shown as a mean±standard deviation (SD).

Phytochemical screening was conducted to evaluate the secondary metabolite of GS extract and flavonoids, alkaloids, saponin, steroids, polyphenol, mono- and sesquiterpene were observed. Saponin acts as an antimicrobial agent, improving wound contraction and the rate of epithelization [15]. Polyphenol accelerates tissue regeneration and also acts as an antiseptic agent against infection. Furthermore, it is used as an astringent to increase rates of wound contraction and epithelization [16].

CMC, which is similar to other natural polymers, was used in this study due to its cross-linking ability to form hydrogel under suitable conditions [17], while carbomer was used due to its wide use in commercial gel preparations [18]. Propylene glycol was used as a moisturizer and enhancer improving the solubility of the active substance in the stratum corneum and drug diffusion through the skin [19]. In addition, triethanolamine was used to neutralize gels containing carbomer after dispersed into water. The hydrogen bonding and ionization of the carboxyl group occurred in the pH range 6.0–8.0 leading to gel formation [13]. To prevent gel degradation, methylparaben and propylparaben, ethylenediaminetetraacetic acid (EDTA) and sodium metabisulfite were used as preservatives, chelating agents and antioxidant, respectively [20-22].

The result of pH measurements of GS extract gel are shown in the following fig.:
This result showed that GS extract gel reduced the erythema caused by burn wounds. Its saponin content can be attributed to the reduction of inflammation due to decreased erythema [26]. This study examined the activity of GS extract on the burn healing process in gel formulations. The extract was successfully formulated into gel preparation using carbomer and HPMC as stabilizers. In vivo study showed GS extract gel could increase the rate of the wound healing process. This study provides fundamental insight into optimizing the gel formulation of extract as a topical preparation to improve the burn wound healing process.

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**AUTHORS CONTRIBUTIONS**

All the authors have contributed equally.

**CONFLICT OF INTERESTS**

Declared none

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