

Review:Pegagan (*Centella asiatica L*) as a Potential Wound Healing Preparation

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Abstract:

Background: Pegagan (*Centella asiatica L*) is also known as Gotu Kola. *Centella asiatica (L.) Urb* belongs to the order Apiales and the genus *Centella L.* (Integrated Taxonomic Information). Asiaticoside and madecassoside acid contained in pegagan function as epithelialization of the injured area. Pegagan contains alkaloids, tannins, flavonoids, alkaloids, steroids, and triterpenoids. This plant is also known to have low toxicity and can be digested in the body. Pegagan is often used for wound healing. Many studies and commercial products use pegagan as a wound healer. The purpose of this journal review is to provide information about various dosage forms of pegagan (*Centella asiatica*) as a wound-healing preparation by describing the benefits of pegagan, the active compound content, activities and preparations of pegagan in the pharmaceutical field as well as the determination of the active compound asiaticoside pegagan.

Key Word: Pain; Pegagan; Wound.

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I. Introduction

Centella asiatica (L.) Urb belongs to the order Apiales and the genus *Centella L.* (Integrated Taxonomic Information). Asiaticoside and madecassoside acid contained in pegagan function as epithelialization in the injured part¹. Pegagan has potential because all parts of it can be used for open wounds, burns, treatment of keloids, leg ulcers, phlebitis, scleroderma, lupus, leprosy, cellulitis, and canker sores². Pegagan is also widely used in pharmaceutical and non-pharmaceutical preparations.

Active compounds of Pegagan

There are lots of active compounds contained in the pegagan herb and each of the active compounds has a variety of activities.

Tabel no 1: Active Compounds of Pegagan

Reference	Active compounds	Activities
3	saponins	Antibacterial
4	Alkaloids	Antidiabetic
5	flavonoids	Antihyperuricemia
6	triterpenoids	Wound healing, antioxidant
7	Steroids	Antibacterial

The pegagan plant contains lots of active compounds such as saponins that act as an antibacterial against the growth of *streptococcus mutans* bacteria. Saponins play a role in increasing the permeability of cell membranes which can change the structure and function of the membrane of *Streptococcus mutans* bacteria. Saponins can interfere with the ability of bacteria to interact with membranes. The content of saponins that are effective against *Streptococcus mutans* bacteris is 80%³. The alkaloids in pegagan have an antidiabetic activity that can reduce blood glucose levels and play a role in inhibiting glucose absorption in the intestine and increasing glucose transport in the blood. The concentration of pegagan used containing alkaloids is 40%⁴. Flavonoids are one of the compounds in pegagan which have activity as anti-hyperuricemia. The flavonoids contained quercetin and kaempferol which functioned as lowering uric acid in the blood in a study⁵, using 70% ethanol extract of pegagan. Triterpenoids help wound healing wherein these triterpenoids there are asiaticoside compounds that play an important role in the skin to strengthen skin cells and smooth blood flow. Triterpenoids are also used as anti-leprosy drugs⁶. Steroids have antibacterial activity that can inhibit the growth of *Staphylococcus aureus* bacteria which can damage bacterial cell membranes and at concentrations of pegagan 60%,80%,100%⁷.



Figure 3: Burning wound¹⁵

2. Incision wound

Incision wounds are wounds that are intentionally made by making clean cuts using sharp objects, incision wounds or it can also be called surgical wounds during surgery which can cause infectious complications with a percentage of 14%-16%¹⁰. Incision wounds if not handled properly and correctly will result in healing or wound closure will not be achieved perfectly¹².



Figure 4: Incision wound¹⁶

3. Acute cuts

An incision wound is an acute type of wound caused by sharp objects resulting in damaged skin and loss of body tissue and will result in bleeding that involves hemostasis and inflammation can occur in the end¹⁷.

Wound healing process

Wound healing has several complex processes and goes through several phases (inflammatory phase, proliferative phase, and remodeling phase). Wound healing can be said to be successful with good results if each phase is fulfilled or passed¹⁸. The inflammatory phase consists of an early and late inflammatory phase where the injured tissue will cause blood vessels to break and cause bleeding. The body will respond to stop bleeding by activating intrinsic and extrinsic coagulation factors. The final inflammatory phase begins on day 5 after injury. The purpose of this final inflammatory phase is to remove dead tissue and prevent infection by pathogenic microbes and prevent colonization¹⁹.

The proliferative phase occurs on the 3rd to 14th day post-traumatic. In this phase, there is a balance between scar tissue formation and tissue regeneration (new blood vessels, fibroblasts, macrophages, and other tissues). The last phase of the healing process is the maturation (remodeling) phase which occurs on the 21st day (up to 1 year). In this phase, new tissue is formed as a wound filler, scar tissue formation, and epithelial growth. The wound healing process is also related to biochemical and cellular responses and involves a complex and dynamic process both locally and systematically¹⁹.

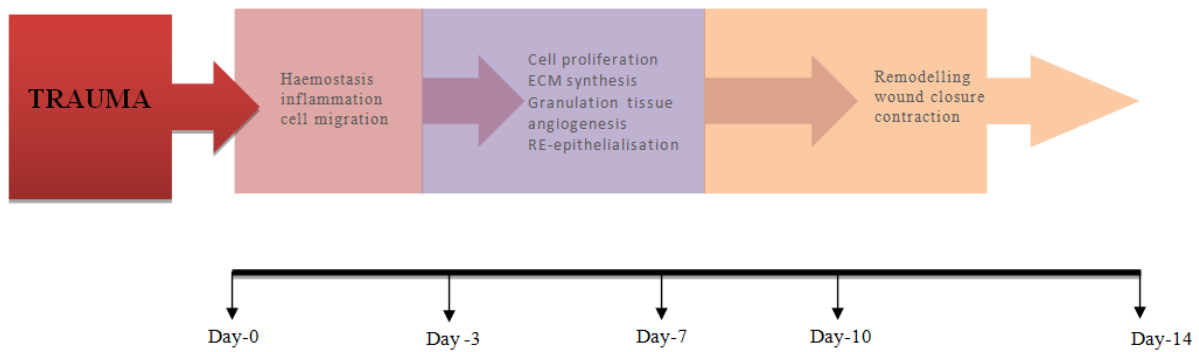


Figure 5: wound healing process

Wound healing formulations

Several preparations with pegagan as an active ingredient for wound healing, such as gels, ointments, and hydrogels

a. Gel

Tabel 1: Formulation gel

Preparation	Ingredients	Effect of Pegagan	Content	Reference
Gel 1	Pegagan extract Papaya leaf extract Propylene glycol NA-CMC Methylparaben Propylparaben Aqua	The effect of Pegagan in combination with papaya leaves at a concentration of 5% can accelerate wound healing.	5%	²⁰
Gel 2	Pegagan extract HPMC Methylparaben Propylene glycol Propylparaben Aqua	The addition of HPMC gelling agent to the Pegagan extract has an effect on the physical properties of the gel and accelerate wound healing with low HPMC concentration	8%	²¹
Gel 3	Pegagan extract Aloe vera extract NA-CMC Glycerin Methylparaben Propylene glycol Aqua	At a concentration of 15%, the combination of pegagan extract with aloe vera most affected the accelerate of wound healing	15%	²²

In the table above there are various pegagan gel formulations from different studies. Each study varied the concentration of pegagan differently. From the results of the first research formulation where a combination of pegagan extract and papaya leaf extract was obtained, it was found that papaya can be used for wound healing because it contains polyphenolic compounds, saponins, and flavonoids. Saponins encourage the formation of collagen while flavonoids and polyphenols have antiseptic activity²⁰. The second formulation is the use of HPMC (hydroxypropyl methylcellulose) as a hydrophilic polymer for topical and oral drug administration. HPMC has the characteristic that is having gel strength with a temperature range of 60-90 C. Judging from polymer substitution, water content concentration, and the use of different HPMC concentrations, data shows that this has no effect on changes in odor and color. When the use of HPMC gelling agent concentration is lower, the healing time of burns will be faster with an optimum concentration of 8%²¹. In-gel formulation 3, a combination of aloe vera (has antibacterial and antibiotic activity) and pegagan (has antioxidant activity) was made. Aloe vera contains vitamins C and E as well as anthraquinone compounds that can relieve pain²², it can be concluded from the three studies that the highest concentration is the one that contributes to the speed of wound healing.

b. Ointment

Tabel 2: Formulation ointment


	Ingredients	Effect of Pegagan	Content	Reference
Ointment 1	Pegagan extract Vaseline Album Adeps lanae	The concentration of pegagan extract affects the physical appearance of the ointment preparation and accelerates wound healing	16%	⁸
Ointment 2	Pegagan extract Vaseline Album	The effect of the concentration of pegagan ointment extract can help	5%,10%	²³

	Nipagin Anhydrous Lanolin	wound healing at concentrations of 5% and 10% which are more effective for wound healing		
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From the formulation of ointment 1, it is known that if the concentration of pegagan is higher, it will affect the color of the preparation (getting thicker)⁸. While in the preparation of ointment 2 there are differences in formulation, especially the addition of anhydrous nipagin and lanolin as preservatives²⁴. The two ointment formulations have different concentrations. The length of the wound is decreasing day by day. The length of the wound that healed the fastest was in the group with a concentration of 16% with an average wound healing time of 7.6 days⁸. In the second journal formulation, the diameter of the surgical wound is decreasing day by day with the most effective concentrations in terms of speed of healing of surgical wounds in the pegagan herbal extract ointment, namely 5% and 10%²³.

c. Hydrogel

Tabel 3: Formulation Hydrogel

	Ingredients	Effect of Pegagan	Content		Reference
Hydrogel 1	Pegagan Faction Polyethylene glycol 400 Polyvinyl Alcohol Silica gel Ethyl acetate Methanol	Hydrogel preparations containing pegagan affect wound diameter	Pegagan Extract		²⁵
Hydrogel 2	Hydrogel pegagan	Hydrogel preparations can affect the number of leukocytes in the wound as a wound cover	Pegagan Extract	-	²⁶

Hydrogels can help reduce the diameter of the wound and reduce the number of leukocytes. In the first hydrogel with 12 days of observation, it was found that the diameter of the wound was gone and there were signs of dry scar formation. Therefore, treatment using a hydrogel containing pegagan showed a better-wound reduction. Hydrogels are moisturizing the skin, treat wounds, and are safe and biocompatible with good physicochemical properties which are also suitable for application in topical wound healing²⁵. In the second hydrogel preparation, the researchers looked at the number of polymorphonuclear leukocytes (PMN), which were the first cells to go to the injured site. These leukocytes act as bacterial phagocytosis which was observed from the post-injury day until the 14th day and then the number of leukocytes was measured. It was obtained data that the number of leukocytes decreased because pegagan leaves contain an essential oil which functions as an antibacterial to slow the growth of bacteria, therefore leukocytes will also decrease²⁶.

Identification of asiaticoside compounds

The identification of asiaticoside can be done using instruments such as Fourier transform infrared spectroscopy (FTIR), mass spectrometry liquid chromatography (LC-MS), High-Performance Liquid Chromatography (HPLC), Thin Layer Chromatography.

a. Fourier transform infrared spectroscopy (FTIR)

The FTIR spectrum determines the absorption band, in the figure below shows asiaticoside in the 918 and 970 cm absorption bands originating from $-(CH_2)$ and at 1060 cm, 1641 cm, 290 cm, and 3273 cm from $-CO$, $-C=O$, CH and $R-OH$ ²⁷.

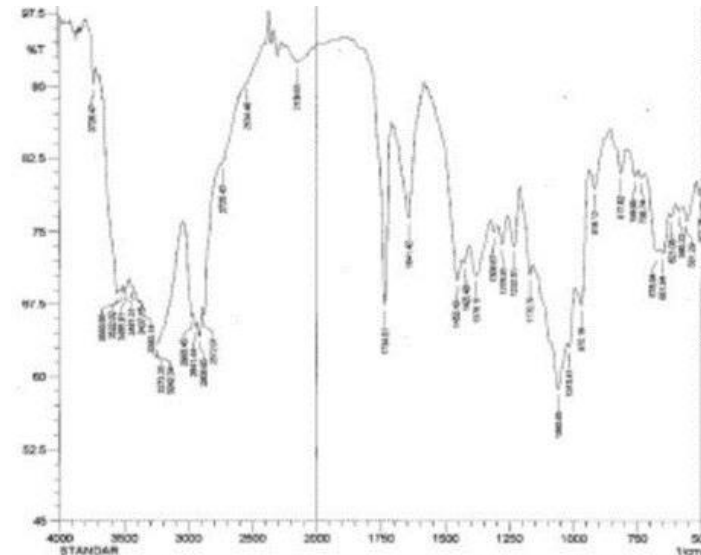


Figure 6: FTIR spectrum of Asiaticoside²⁷

b. Liquid chromatography-mass spectro (LC-MS)

Identification using the LC-MS instrument can detect compounds that are more specific in the molecular form of a compound to be identified. The first step that must be done is making the extract and then macerating (to separate the active compounds). The parameters of the LC-MS method are LOD (linearity of detection limit and LOQ (linearity of quantitation limit), linearity, namely how the ability of the analytical method responds to the analyte concentration in the sample, selectivity and the detector used with the ability to detect asiaticoside compounds at a time range of 3.37 -3.38 separates asiaticoside²⁸.

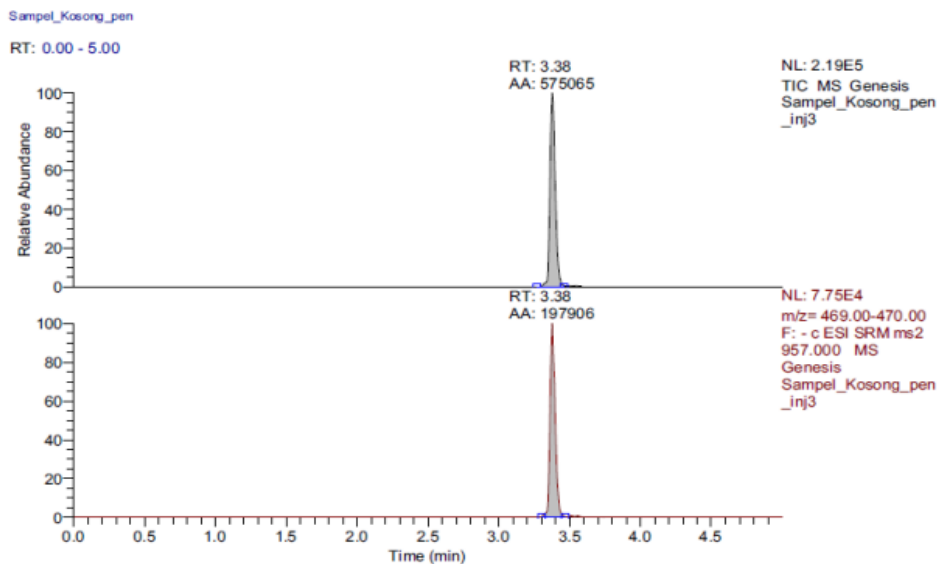


Figure 7: Chromatogram of asiaticoside²⁸

c High performance liquid chromatography (HPLC)

HPLC is used to find out based on its retention time by looking at the chromatogram of the asiatica extract sample that appears in the 8.2 min²⁹

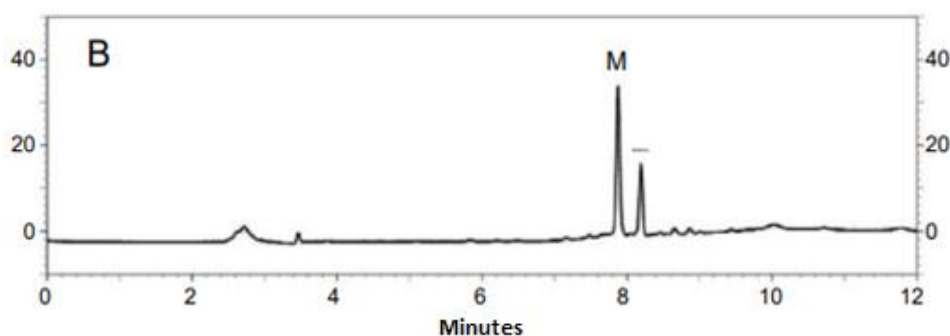


Figure 8: Chromatogram Asiaticoside by HPLC²⁹

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