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Plants potential to be developed for wound healing medicine in Indonesia

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Abstract

Wound healing is a complex process of tissue repair consists of four stages: hemostasis, inflammation, proliferation, and remodeling. These stages are influenced by different chemicals so that the use of natural products containing many lead compounds is important to be considered. In the plant-derived natural products there is a variety of useful chemicals for wound healing process such as: antioxidants, antimicrobials, anti-inflammatory agents, and enhancers for re-epithelialization and collagen formation. That's the reason why research on the discovery of new wound drugs from natural products, including in Indonesia, keeps increasing. This review paper presents the results of research on the potential of plants in Indonesia that can be developed into wound healing drugs that have been published in the last 10 years.

Keywords: Plant-derived medicine; Wound healing drugs; Indonesian plants; Anti-wound ingredient; Phyto medicine

1. Introduction

Due to failure of modern drug discovery methods to deliver various lead compounds for curing disease, recently many big pharmaceutical companies have renewed their interest in natural product, instead of favor synthetic compounds [1-2].The global drug market is worth 1.1 trillion dollars and 35% of the medicines originated from natural products [3].Natural products, with today's technological advances, can be screened and processed in discovering new drugs [4].

In the context of wound treatment, both cuts and burns, the search for natural product-based medicines is very relevant considering that wound healing is a complex process of tissue repair [5]. Cutaneous wound healing is consisted of 4 stages: hemostasis, inflammation, proliferation, and remodeling [6]. Hemostasis is mechanism of bleeding cessation from blood vessel characterized byvascular constriction, platelet aggregation, degranulation, and fibrin plug formation. Inflammation is a wound healing stage characterized by neutrophil infiltration, monocyte infiltration and differentiation to macrophage, lymphocyte infiltration. Proliferation is a stage in which the wound is rebuilt with new tissue made up of collagen and extracellular matrix characterized by re-epithelialization, angiogenesis, collagen synthesis, and ECM formation. Remodeling is a phase when collagen is remodeled, vascular maturation, and the wound fully closes [7].

The advantage of natural products, medicinal plant-derived ingredients, for instance, is that they contain a variety of useful chemicals for wound healing process such as: antioxidants, antimicrobials, anti-inflammatory agents, and enhancers for re-epithelialization and collagen formation [8].

The study reported by Sharma et al. (2018) prove this assumption, that polymolecular traditional medicine has more therapeutic benefits than a single molecule based allopathic medicine in wound care because they are not only anti-inflammatory and anti-microbial in nature but also affect tissue regeneration and rejuvenation. The wealth of active

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ingredients in these natural products allows the wound healing process to be faster because inflammation, epithelization, vascular maturation, and wound closure can be shortened [9].

In addition to these scientific-technical reasons, the rise of research on the discovery of new wound drugs from natural products, including in Indonesia, is the phyto-medicines cost relatively economical and inexpensive [10]. This paper presents the results of research on plants in Indonesia that have the potential to be developed into wound healing drugs carried out by researchers in this country in the last 10 years.

2. Data collection

The research results collected in this paper are those that have been published in scientific journals, both domestically and internationally, which can be searched through the Google search engine. The criteria for the works to be collected are publications between 2012 -2022, both in reputable journals or ordinary ones. In addition, most importantly, the plants used as test materials are plants that grow in Indonesia.Here is (Table 1) the list of plant species that shown efficacies in wound healing revealed by Indonesian researchers.

Table 1 Plant species that have been tested for their effect on wound healing in Indonesia

Plant species	**Type of extract**	**Test animal**	**Type of wound**	**Healing parameter**	**Ref.**
Anredera cordifolia(Ten.) Steenis	ethanolic leaf-extract in vaselin base ointment	rats (Rattus norvegicus)	skin burns from iron hot plate	histological (PMN infiltration, collagen deposition, fibrosis, and angiogenesis)	[11]
	water leaves extract paste	Mice (*Mus musculus* L.)	incision wounds	percentage of wound contraction	[12]
	ethanolic leaf-extract ointment	Guinea pigs	excision wounds	percentage of wound closure	[13]
	ethanolic leaves extract ointment	hyperglicemic male and female rabbits	excision wounds	wound closure and proliferation of fibroblast cell	[14]
	leaves extract combined with MEBO	Human: a woman patient	burns wound from hot cooking oil	rate of epithelialization and infection	[15]
Ageratum conyzoides L. combined with *Centella asiatica*	Ethanolic leaves extract	albino mice (*Mus musculus*)	incision wounds	percentage of wound closures	[16]
Allium sativum L.	water and ethanol extract ointment	*Mus musculus* L.	burns wound from hot metal plate	rate of healing phases, percentage of wound closures	[17]
Aloe vera combined with *Melastoma polyanthum*	gel containing ethanol extract	male white rats (*Rattus norvegicus*)	burns wound from hot iron plate	diameter ofwound closures	[18]
Cassia alata L.	methanolic leaves-extract ointment	male rabbits	excision wounds	scores of wound closures	[19]

Centella asiatica	ethanolic leaves extract ointment	hyperglicemic male and female rabbits	excision wounds	wound closure and proliferation of fibroblast cell	[20]
Colocasia esculenta L.	ethanolic leaf stalk extract ointment	*Mus musculus* L.	burns wound from hot iron plate	diameter ofwound closures	[15]
Cocos nucifera (coconut)	virgin coconut oil (VCO)	rabbits (*Oryctolagus cuniculus*)	burns wound from hot metal plate	epithelialization and neovascularizatio n	[21]
Chromolaenaodorata L.	ethanolic leaves extract ointment	wistar rats (*Rattusnorvegicus*)	burns wound from hot metal plate	percentage of wounds closures	[22]
Euphorbia tirucalli	ointmentcontainin g ethanol extract	Wistar rats (*Rattus norvegicus*)	burns wound from hot iron plate	rates of inflammation, proliferation, and remodeling phases	[23]
Ficusdeltoidea	paste containing methanolic leaf extract	male mice (*Mus musculus*)	incision wounds	percent wound closures and content of DNA and hydroxyproline	[24]
Impatiens balsamina	ethanolic leaves extract ointment	wistar rats (*Rattusnorvegicus*)	excision wounds	inflammatory cells count and collagen formation	[25]
Melaleucacajuputi	gel containing methanolic flower extract	wistar rats (*Rattusnorvegicus*)	excision wounds	wound closures	[26]
Musa acuminate (banana)	ethanolic leaf sheath extracts	male rabbits	burns wound from hot metal plate	wounds diameter and closures	[27]
Poikilospermumsuaveolen si	ethanol and ethylacetate leaves-extract	albino wistar rats	excision wounds	percentage of wound closures	[28]
Piper nigrum L. combined with *Coffeacanephora*	ethanol and ethylacetate leaves-extract	albino wistar rats	excision wounds	percentage of wound closures	[29]
Plantago major	Gel containing ethanol leaf extract	hyperglycemicwista r rats	Excision wounds	nitric oxide production and fibroblast cells proliferation	[30]
Saurauiavulcani, Korth.	water infusion extract ointment	hyperglycemia rats	excision wounds	percentage of wound closures	[31]

Stigma maydis	ethanolic leaves extract gel	white rats	hot metalburn s wound	percentage of wound closure and collagen formation	[32]

3. Common approaches in wound medicine efficacy test

Inferring idea of Najmi et al (2019) regarding approaches in the discovery and development of plant-based natural products, the approach applied by Indonesian researchers in finding and testing plant-based wound medicines is mostly traditional and conventional.Plant selection is based on the observation, the empirical experiences related to the use of the plants, description and experimental analysis of traditionally used plant materials [33].The preparations used are mostly still crude extracts which are presented in the form of a paste, gel, or liquid that is rubbed on the wound. The organisms used in the assays are generally mammals, rarely in humans. Types of wounds treated are incision, excision, and burns. The wound healing parameters measured are mostly anatomical parameters. Several used histological, cellular and sub-cellular parameters.

4. Conclusion

In summarize, there are at least 20 species of plant grown in Indonesia that are revealed to have potency as wound healing. These plants are: *Anredera cordifolia, Ageratum conyzoides, Allium sativum, Aloe vera, Cassia alata, Coffea canephora, Colocasia esculenta, Cocosnucifera, Chromolaena odorata, Euphorbia tirucalli, Ficus deltoidea, Impatiens balsamina, Melaleuca cajuputi, Melastomapolyanthum, Musa acuminata, Poikilospermum suaveolens, Piper nigrum, Plantago major, Saurauiavulcani,* and *Stigma maydis.*

However, the data presented in this article only summarizes some of the research results that have been officially published in scientific journals that can be accessed via the internet. If all research results in various universities, both by lecturers and students are considered, the trend of research on natural medicines in Indonesia is very high. Therefore, in the future, research on the search and development of natural wound medicines needs to be accompanied by strict quality, safety, efficacy and standardization tests.

Compliance with ethical standards

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Disclosure of conflict of interest

Author declared there is no competing interest.

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