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Wound Healing Studies of Selected Euphorbia Species: A Review

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ABSTRACT

For thousands of years, nature has been the source of medicine, and a huge number of modern marketed drugs which isolated from natural remidies were discovered depending on its useses in traditional medicine. Wound healing possesses is still the great challenge for the medical community. According to the WHO, more than 80% of world population utilized traditional remedies as alternative medicine for wound healing treatment . This work focus on the Euphorbia species plants (belong to Euphorbiaceae family) which have wound healing activity. Published previous studies on the wound healing property of Euphorbia species plants was gathered by the use of different scientific websites such as Google Scholar, PubMed, Science Direct, and Web of Knowledge. This review identified plants from species of Euphorbia that promote wound healing. The selected plants are with high content of flavonoids, saponins, steroids, triterpenoid and tannins. At the same time these components reportedly promote wound healing by different pharmacological activity like mopping of reactive oxygen species from wounded tissues, inhibition / cidal effects against infections that delay wound healing and anti-inflammatory activities. These plant could be considered as future drug candidates for wound healing for healing of wounds.

KEYWORDS: Wound healing, Euphorbia, Euphorbiaceae

INTRODUCTION:

wound was defined as physical, chemical or thermal injuries that cause an opening or breaking in the integrity of the skin(Shenoy et al., 2009). In other words, wound is a breakdown in the epithelial integrity of the skin and may be accompanied by disturbance of the structure and function of underlying normal tissue and may also result from a contusion, haematoma, laceration or an abrasion(McGready et al., 2001, Dewangan et al., 2012). It range from a simple break in the epithelial integrity of the skin to deeper extending into subcutaneous tissue. It might include destruction to other structures such as tendons, vessels, nerves, muscles, parenchymal organs and bone(Velnar et al., 2009).

Wounds can be characterized as acute and chronic according to their healing time frame(Majumdar et al., 2007, Manuskiatti and Maibach, 1996). Wounds that repair themselves ordinarily by following a timely and orderly pathway with the end result of both functional and anatomical restoration are categorized as acute wounds. Commonly the time sequence of healing ranges from 5 to 10 days or within 30 days. Chronic wound is the skin injury that unsuccessful to heal through the normal stages of healing and cannot be repair in an orderly and timely manner. The healing process of chronic wound is disturbed by various factors that prolong one or more stages of healing. These factors include infection, necrosis, exudate, tissue hypoxia, and superfluous levels of inflammatory cytokines(Velnar et al., 2009). The process of normal wound healing can be categorized into four stages(Guo and

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DiPietro, 2010) which consist of coagulation and haemostasis, inflammatory, proliferation, and remodeling phase characterized by scar tissue formation which eventually determines the strength and appearance of the tissue(Velnar et al., 2009, Brown, 2015) . In normal healing process, all four phases must occur in well-ordered way. Many factors can delay or interruputed one or more phases of this process which causing impaired wound healing(Brown, 2015, Dryden et al., 2013) (16,17).Some of these factors are improper diet, infection at wound site, drugs, elderly age, dibetes and other disease conditions(Guo and DiPietro, 2010).

Euphorbiaceae is considered one of the largest families of the plant kingdom,it is mostly monoecious herbs, shrubs, and trees. It comprises about 300 genera and 7,500 species that are further characterized by the frequent occurrence of milky latex. A number of plants of the Euphorbiaceae are of considerable economic, medicinal importance and many are grown as ornamental plants This family is commonly distributed in the tropics and sub-trobic area, with the most species in the Indo-Malayan region and tropical America. (Schmelzer et al., 2008).

The genus Euphorbia is the largest in the plant family Euphorbiaceae, consisting about 2000 known species. These species are spread in tropical and non-tropical areas such as the the Middle East, Mediterranean, South Africa, and southern USA(Jassbi, 2006, Shi et al., 2008).
In addition, this genus related to the family that is well acknowledged for the chemical diversity of their isoprenoid constituents. Euphorbia is reported to have phloracetophenones , cerebrosides, glycerols, sesquiterpenoids, steroids, and flavonoids. Some species of the genus Euphorbia are used in folkloric medicines to cure skin disorders, gonorrhea, intestinal parasites, migraine and wart(Ertas et al., 2015). The latex of these plants contains numerous natural compounds, some of which are of therapeutic importance or of commercial use(Giner and Schroeder, 2015). Few Euphorbia species have also been reported for wound healing potential(Goyal et al., 2012). In this paper, we are reporting the wound healing studies of some Euphorbia species growing in trobical and subtrobical counteries.

MATERIAL AND METHODS:

Electronic databases including PubMed, Scifinder® and Google Scholar were searched for Wound healing stdies of selected Euphorbia species between 1990 and 2020. All filtered articles were considered to determine any validated in vitro or in vivo wound model. Included articles were reviewed concerning plant botanical names, the parts of plants used in the particular study and studied nature of plant extracts, active compounds or constituents and wound models used, if it is in vivo or in vitro. Also it included the standardized clinical trials with obviously demonstrated wound healing activity in the models used. The authors looked for significant differences between control group and test group and with respect to wound tensile strength, wound contraction, period of epithelialisation, neovascularization, keratinization, collagenation, and fibrosis.

RESULTS AND DISSCUSSION:

Phytoconstituents in euphorbia species support wound healing activity

Several research across the world have shown that phytochemicals may play a serious role in preventing and/or treating a number of diseases and many 0f these have medicinal benefits for wound healing and skin

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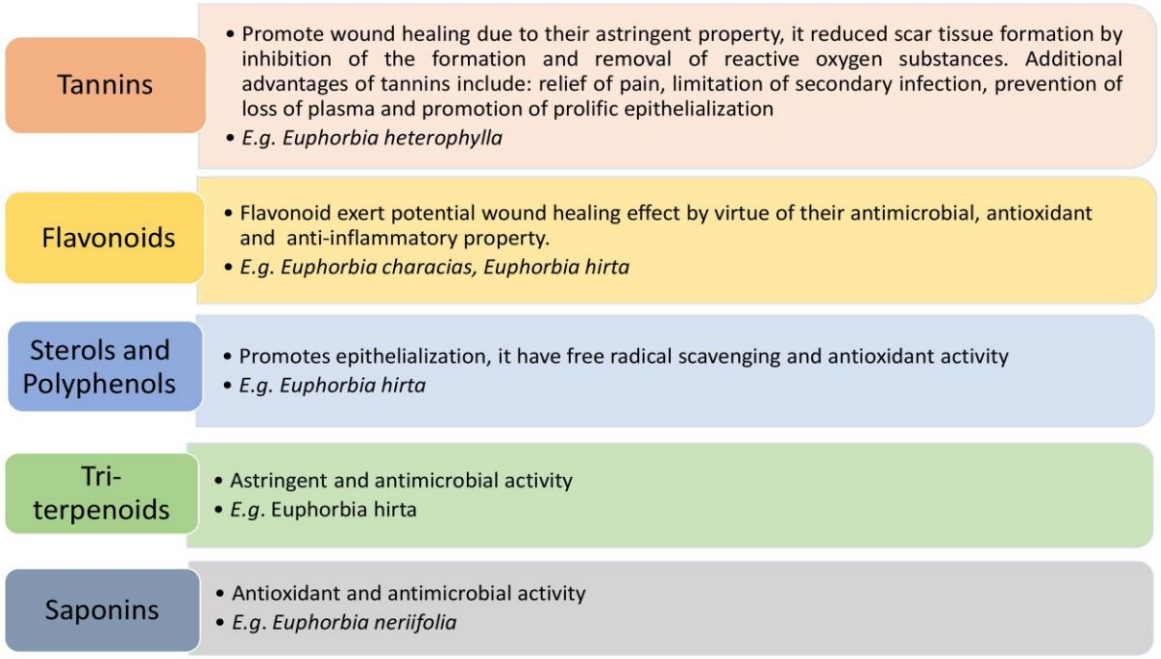
regeneration(Wim Vanden and Guy, 2010). Phytoconstituents present in the plant extracts have been widely used as topical applications for wound healing(Deriso and Hsu, 2010). It may affect one or more phases of the wound healing process in a positive manner in proper sequence. Plants from the genus Euphorbia have been found to contain different phytoconstituents like tannins (euphorbins), triterpenoids (lupeol, lupeol acetate, β-amyrin and betulin) and phytosterols such as β- sitosterol have also been reported(Al-Snafi, 2017). The flavonoids kaempferol, myricetin, rutin, quercetin, and their derivatives and phenolic compounds have been found(Noori et al., 2009), along with the volatile compounds α terpineol, α-humulene, linalool ,β-caryophyllene, terpinene, and germacrene-D(Fokialakis et al., 2003). The diterpenoids with the basic skeletons of jatrophane, lathyrane, and myrsinane(Sulyok et al., 2011) ; daphnane, ingenane and tigliane(Jassbi, 2006) ; pepluane, paraliane, and segetane. The sesquiterpenoids euphanginol, euphorbioside A, euphorbioside B, and clovandiol have also been reported(Shi et al., 2008). Digram (1) show various substances having wound healing activity that isolated from plants e.g. tannins , polysaccharides, flavonoid, sterol etc(Ghosh and Gaba, 2013).



Digram (1) Show phytoconstituents from euphorbia species and their role in wound healing:Tannins; Euphorbia heterophylla(James et al., 2010), Falvonoid; Euphorbia characias (Ozbilgin et al., 2018), Euphorbia hirta (Bigoniya et al., 2013), Sterols and Polyphenols; Euphorbia hirta (Bigoniya et al., 2013), Tri-terpenoids; Euphorbia hirta (Al-Snafi, 2017), Saponins; Euphorbia neriifolia (Bigoniya and Rana, 2007).

Pharmacological activities of euphorbia plants that supporting wound healing

Anti- inflammatory activity

In normal wound healing process, the Inflammation phase is essential, because in this phase a type of white blood cells called neutrophils that are responsible for microbial clearance in the area of the wound (phagocytosis) as it playing a role in antigen appearance. Also in this phase production of growth factors and inflammatory cytokines occurred . So any pathological process that affects with this self-limited physiological process can result in a non

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healing wound because of net destruction of soluble growth factors and matrix elements(Lan et al., 2013, Pierce, 2001). Many animal studies proofed the anti-inflammatory effect of plant extract thus can be used as wound healer drugs (Mascolo et al., 1987, Akihisa et al., 1996).

Antioxidant activity

The Plants produces many antioxida2nt compounds that are important to neutralize reactive oxygen species (ROS) in order to survive. ROS include non free-radical species such as hydrogen peroxideetc and free radicals species such as superoxide anion radicals, hydroxyl radicals, these are important mediaters of signaling and inflammation in wound repaired, so any abnormal low levels of these antioxidants have been associated with impaird wound healing(Shahriar, 2013). Various antioxidant natural compound were derived from plant such as flavonoids, tannins, polysaccharides , lignans , etc.. that possess wound healing by scavenging free radical and promoting collagen synthesis(Sen et al., 2002).

Antimicrobial activity

Microbial infections play a significant role in impaired healing of the wounds and can caused development of infection-related complications(Misic et al., 2014, Robson, 1997). Many of herbal plants containing antimicrobial compound have been scientifically showed to possess wound healing activity such as tannins,cumarin etc..(Patel et al., 2011).

Analgesic activity

Pain have negatively impact on wound healing. It can cause interruption in wound healing process by dysregulating neuroendocrine and immune functions which play critical role in wound repair mechanism(Mudge and Orsted, 2010). Nomber of the herbal preparations possessing analgesic and anti-inflammatory activities can be active for pain management of wounds(McGuire et al., 2006). Table 1 show the Euphorbia species plants with there pharmacological activity that support the wound healing.

Table (1): Show studies related to some of Euphorbia species plants with there pharmacological activity that support the wound healing:

Activity	Plant name	Refrence
Anti-inflammatory	***Euphorbia hirta***	**(Sharma et al., 2014, Al-Snafi, 2017)**
	Euphorbia Aegyptiaca	**(Abo-Dola and Lutfi, 2016)**
	Euphorbia dracunculoides	**(Majid et al., 2015)**
	Euphorbia retusa	**(Sdayria et al., 2018)**
	Euphorbia acaulis	**(Singh et al., 1984)**
	Euphorbia nicaeensis	**(Cateni et al., 2004)**
	Euphorbia Antiquorum	**(Saikia, 2016)**
	Euphorbia helioscopia	**(Park et al., 2001)**
Antioxidant	***Euphorbia hirta***	**(Sharma et al., 2014, Al-Snafi, 2017)**
	Euphorbia dracunculoides	**(Majid et al., 2015)**
	Euphorbia retusa	**(Sdayria et al., 2018)**
	Euphorbia golondrina	**(Lawrence Monah et al., 2016)**
	Euphorbia mili	**(Besagas and Gapuz, 2018)**
	Euphorbia trigonaa	**(Besagas and Gapuz, 2018)**
	Euphorbia antiquorum	**(Besagas and Gapuz, 2018, Saikia, 2016)**
	Euphorbia helioscopia	**(Maoulainine et al., 2012, Uzair et al., 2009)**
	Euphorbia tirucalli	**(Munro et al., 2015)**
	Euphorbia tithymaloides	**(Saikia, 2016)**
	Euphorbia wallichii	**(Tantary et al., 2016)**
	Euphorbia cyparissias L	**(Stankovic and Zlatic, 2014)**
Analgesic	***Euphorbia dracunculoides***	**(Majid et al., 2015)**
	Euphorbia retusa	**(Sdayria et al., 2018)**

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	Euphorbia hirta	**(Al-Snafi, 2017)**
	Euphorbia prostrata	**(Kiprop, 2015)**
	Euphorbia royleana	**(Bani et al., 1997)**
Antimicrobial	***Euphorbia golondrina***	**(Lawrence Monah et al., 2016)**
	Euphorbia Antiquorum	**(Saikia, 2016)**
	Euphorbia helioscopia	**(Uzair et al., 2009)**
	Euphorbia hirta	**(Al-Snafi, 2017)**
	Euphorbia aleppica	**(Kirbag et al., 2013)**
	Euphorbia szovitsii	**(Kirbag et al., 2013)**
	Euphorbia falcata L	**(Kirbag et al., 2013)**
	Euphorbia denticulata	**(Kirbag et al., 2013)**
	Euphorbia macroclada Boiss.	**(Kirbag et al., 2013)**
	Euphorbia cheiradenia	**(Kirbag et al., 2013)**
	Euphorbia virgata	**(Kirbag et al., 2013)**
	Euphorbia petiolata	**(Kirbag et al., 2013)**

Wound healing studies of some euphorbia spiecies

Various pharmacological reports are carried out on different plant species employing different wound healing models and its underlying molecular mechanism for the confirmation of their traditional claims and development of safe and effective and globally accepted herbal drugs for wounds.

Euphorbia species

Serkan Özbilgin et al. study the effect of n-hexane, ethyl acetate, and methanol extracts of some species of euphorbia arial parts (*E. characias subsp. wulfenii, E. helioscopia, E. macroclada, E. seguieriana subsp. seguieriana* and *E. virgata. Linear*) on rats with incision, circular excision wound modele.The hydroxyproline assay method were used to assess the wound-healing activity. The results show the that the methanol extract of the aerial parts of E. characias subsp. wulfenii have a 65.24% reduction in the area of the wound by day 10 for the circular excision model wound-healing activity with 43.03% tensile strength for the linear incision wound model The tissue treated with this extract also was found to contain 35.47 µg/mg of hydroxyproline(Özbilgin et al., 2018).

Sarfaraz Ahmed et al. study the preliminary wound healing activity of five species of Euphorbia (*E. consorbina 1, E. consorbina 2 , E. balsamifera, E. inarticulata* and *E. schimperi*). The study carried out on rats with excision wound modele, the animal were treated topically with ethyle acetate and methanol extracted of each plants at a dose of 400 mg/kg body weight for 20 days. Where the povidone-iodine ointment was used as a reference drug. The period of epithelialization and wound contraction measurement were used to assess the effect of plants extracts on wound repairing. The results show that the methanolic extract of *E. balsamifera* and *E. schimperi* showed the high rate of wound contraction (100%) and decrease in epithelization period 19.00±0.40 and 18.50±0.64 respectively, followed by the methanolic extracts of *E. consorbina* 2, ethyl acetate extract of *E. inarticulata* and ethyl acetate extracts of *E. consorbina* 2 which showed significant ($P < 0.001$) wound contraction and reduction in epithelization period. On the other hand ethyl acetate extract of *E. consorbina 1,E. schimperi* and *E. balsamifera* and the methanol extract of *E. Consorbina 1* and *E. Inarticulata* treated groups was not showing significant wound healing. Also they tested the Methanol extracts of *E. balsamifera* and *E. schimperi* for their safety margin and found safe up to dose of 2000mg/kg body weight. They concluded that the topical application of methanol extracts of *E. balsamifera* and *E. schimperi* have potential wound healing activity which is identical with refrance drug Povidone-iodine(Ahmed et al., 2016).

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Euphorbia hirta

E. hirta, known as ana tera, Em elhaleeb, Asthuma weed, snakeweed and Dudhi is very common among natural and traditional healer.Upadhyay et al. study the invitro antmicrobial,antioxidant and fibroblast proliferating activity of the methanolic extract of the leaves of the *E. hirta* using dermal fibroblaste cell . Also they study the invivo wound healing activity on animals with excision wound modele. The extract show significant fibroblaste proliferation activity (112% at 12ug/ml). Also there study reveals that the methanol extract of the E. hirta possess wound healing activity as it have antioxidant and potentially high anti-microbial activity against *Escherichia coli* and *Klebsiella pneumoniae*. The study, they concluded that the *E. hirta* possess antimicrobial and antioxidant property, increases the fibroblast proliferation and alters the expression of bFGF, COL3A1 and Smad family proteins during wound repair process in granulation tissue, this rationalizing the traditional use of the *E. hirta* in wound healing (Upadhyay et al., 2014).

There is another studies by Papiya Bigoniya et al. study the wound healing of total flavonoid fraction of *E. hirta* on rats with incision, excision and dead space wound model on rat treated orally at constrations 200, 400 and 600 mg/kg. Wound healing was evaluated by rate of wound contraction, tensile strength, epithelisation period, and estimation of granulation tissue weight, hydroxyproline, SOD, catalase and total protein content. The constraton of (600 mg/kg) significantly increased the wound breaking strength, granulation tissue weight and hydroxyproline content ($p < 0.001$). Epithelialize period was quicker and the rate of wound contraction was significantly higher ($p < 0.05$-0.001) in constrations 400 and 600 mg/kg treated groups. They concluded that Increased tensile strength, wound contraction rate and hydroxyproline content provide strong evidence for would heal property of *E. hirta* flavonoid(Bigoniya et al., 2013).

Study conducted by K.Rathnakumar et al.show the wound healing activity of the ethanolic extract of the *E. hirta* leaves on animals with excision wound model, the extract was formulated as an ointment in two different constrations (5% and 10% W/W).The ethanolic extract show significant ($p<0.001$) wound contraction(K et al., 2013).

Jaiprakash B et al. study the burn wound healing effect of the ethanolic extract of *E. hirta* leaves on rat, the extract formulated as cream (2% w/w).The observations of percentage wound closure was made on 4th, 8th, 12th, and16th post wounding days. The result was showed significant burn wound healing activity .By this they concluded the folklore of the use of the plant in the management of burns(Jaiprakash et al., 2006).

There is another study done by Riazul Haque Tuhin et al. study the wound healing effect of *E. hirta* in diabetic rats induced by alloxan. They used ecisional wound modle and animal groups treated either orally by (100, 200 and 400 mg/ kg/day) and another groups treated topically with the extract (5% and 10% ointment 50 mg/kg/day) and 5% povidone iodine ointment 50 mg/kg/day) was used as standard for 16 days. The diabetic wound healing mechanism was studied by measuring the plasma level of glucose, malondialdehyde (MDA) and nitric oxide (NO) in both control and treated groups.The activity, histopathology of the wounds tissues from excision wound model was performed. *E. hirta* caused significant wound closer both orally (35.92%, 44.69% and 61.42% at the doses of 100,

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200 and 400, respectively) and topically (32.86% and 36.32% at the doses of 5% and 10%) treated groups as compared to diabetic control. By this study they concluded that *E. hirta* plant extract promotes healing of wounds more significantly as compared to diabetic control rats, where healing is otherwise late(Tuhin et al., 2017).

Euphorbia Prostrata

E. prostrate, known as prostrate spurge or prostrate sandmat, possesses many actions one of which is for wound healing. Patil et al. study the effect of E. prostrate on excional wound healing model on rats.The study was involved group A and group B had Cream and 1% *E. prostrate* cream applied topically on the excisional wound respectively. Wound healing and epithelisation was assessed on Days 4,8,12,16,20. The results showed that group A had an average wound size of 348±13.0 on day 4, 278±10.5 on day 8, 119±9.8 on day 12, 86±9.2 on day 16 and 100% wound healing was observed day 20 onwards. while group B showed an average wound size of 296±11.0 on day 4, 147±9.5 on day 8 and complete wound healing was observed day 12 onwards in the test group.They conclusion that *E. prostrata* was promise as effective drug therapy for wound healing(Patil and Limaye, 2017).

Euphorbia characias subsp. wulfenii

E. characias subsp. wulfenii is known as Mediterranean spurge or Albanian spurge.The wound healing effect of methanol extract of the aerial parts was studing by sekan ozbingin et. al. on rats with linear incision and circular excision wound model. Anti-inflammatory was also studies. The results showed that *E. characias subsp. wulfenii* have 43.04% activity on linear incisio wound model, 65.24% activity on circular excision wound model and 34.74% anti-inflammatory activity. The concluded from this study the traditional use of the *E. characias subsp. wulfenii* aerial parts as wound healer(Ozbilgin et al., 2018).

Euphorbia caducifolia

E. caducifolia is known as Leafless Milk Hedge ,it is native to Thar Desert of India, where latex of its is used by the local inhabitants for treatment of cutaneous eruption, bleeding wound,and other skin diseases. Manoj Goyal et. al.study the in vitro effect of clotting of platelet free plasma and angiogenesis in chick chorioallantoic membrane (CCM) of the latex of *E. caducifolia*. Excision and incision wounds model were used to study effect of Latex on wound contraction, hydroxyproline and tensile strength and DNA content. The results showed that the latex at the all dose levels. 56.77, 74.48 stimulates the blood vessel formation in CCM, and 78.09% increase in area of angiogenesis was observed in latex concetrations 2.5, 5.0 and 10mg/ml treated groups respectively. The excised skin of the latex in concentrations 5.0 and 10mg/ml treated animals found to have higher content of hydroxyproline and DNA, in compared with control group.There was an acceleration of the wound closure observed with an enhanced number of fibroblasts and collagen content in with latex treated mice. They concluded from the in vitro and in vivo experiments that *E. caducifolia* latex exerts significant wound healing activity, demonstrating its relevant therapeutic potential(Goyal et al., 2012).

Euphorbia heterophylla

E.heterophylla is known as painted euphorbia, Japanese poinsettia, desert poinsettia, wild poinsettia, fire on the mountain, paintedleaf, painted spurge, milkweed, and kaliko plant. It was traditionally used to treat a variety of ailments as laxative, antigonorrheal, migraine and wart cures(Rodriguez et al., 1976, Falodun et al., 2003). James O

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and Friday study the phytoconstituents, bioactivity and wound healing potential of *E.heterophylla* leaf extracts.The last one was formulated as an ointment and it was used for evaluating the wound-healing potential in an excision wound model. The extracts healing activity is comparable to the reference standard (Povidone iodine). The results showed that the ethanol extract of *E.heterophylla* demonstrated a significant increase in protein and exhibited high percentage of wound closure (78.56±0.010 at day 16 and 100% at day 24).They concluded that aqueous and ethanol extracts showed significant wound healing activity when topically administered on rats.These results proven the traditional use of *E.heterophylla* leaf gel for healing wounds(James et al., 2010).

Euphorbia nerifolia

E. nerifolia is known as Milk-hedge, Dog's Tongue. In traditional system, leaves of *E.neriifolia Linn*. are used as aphrodisiac, diuretic, in cough and cold, bleeding piles and ano-rectal fistula(Shi et al., 2008). Papiya Bigoniya, A. C. Rana was study the wound healing activity of the *E.nerifolia* leaves extract on excision wound and dead space wound model along by determination of hydroxyproline, protein catalase and superoxide dismutase in wound granulation tissue. The standard control groups were treated with vitamin C (250 mg/kg, i.p).The results of extract in 200 & 400 mg/kg doses showed significantly ($p<0.05$) enhanced epithelization. Also it showed significantly ($p<0.001$) increases hydroxyproline content, protein content, catalase activity and decreases superoxide dismutase activity in granulation tissue. They concluded that *E. neriifolia* enhances wound contraction and epithelisation. It also increased protein and hydroxyproline content, collagenation with added antioxidant activity on the wound site. These activity may be due to presence of saponins and flavonoids which reduced oxidative stress in wound area and promote healing(Bigoniya, 2007). Another study by Sovan Pattanaik et. al were chose the methanolic extract of the leaves of *Crataeva magna* (CNM) and *E. neriifolia* (ENM) to investigate in excision and incision wound models. The animles were treated topically with methanolic extracts of the two plants at the dose of 500 mg/kg/day. Healing was measured by the rate of wound contraction, time until complete epithelialization, incision breaking strength, estimation of hydroxyproline and histopathological parameters. The results showed that wound contraction was completely closed by both the plants in the study period. In excision and incision wound models, all the test drugs showed significant ($P<0.001$) wound healing activities compared to the control standard drug Framycetin(Pattanaik et al., 2014). The milky latex is used frequently in central India for burn,pile and deep craks in sole of leg(Bigoniya, 2010). A.M. Rasik was study the wound healing activity aqueous extract of the latex of *E. neriifolia* in guinea pig. They produced Surgically cutaneous wounds and treated with topical application of 0.5% and 1.0% sterile aqueous solution of the extract. The results showed that aquous extract of the latex of *E. neriifolia* helped the healing process as demonstrated by increase in tensile strength, DNA content, epithelization and angiogenesis(Rasik et al., 1996).

Euphorbia tirucalli

E. tirucalli L. is known as aveloz, Indian tree spurge, pencil cactus, pencil tree,milk bush and naked lady. The latex of E. tirucalli has been used by native barazil people as traditional medicine as antisiphilitic, anti-helminthic and anti-tumoral(Silva et al., 2007).Barros Filho et al. study the effects of crude extract of E. tirucalli in cutaneous wound healing.the mice trated topically with 0.1 mL (30 mg/mL) hydroalcoholic extract of E. tirucalli while the

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same volume of 0.9% saline solution was applied to the control groups all groups treated for 14 days. The wound healing was evaluated measurining the lesion diameter and after programmed death, a surgical specimen was harvested for histopathology study. The results showed by the macroscopic analysis, no statistically significant difference was observed ($p = 0.120$ and $p = 0.186$, for the 7th and 14th days of death, respectively) and the histological evaluation revealed no statistically significant difference in the variables acute inflammation ($p = 0.014$) and fibrosis ($p = 0.018$), when compared with the control group.they concluded that the crude hydroalcoholic extract of *E. tirucalli.* confirmed better results in the healing process, acute inflammation and fibrosis on the 14 day postoperatively(Barros Filho et al., 2013).

Euphorbia nivulia

E. nivulia is commonly known as milkhedge.S. Gopi Krishnan et al. was study the wound healing activity of methanolic extract of *E. nivulia* in albino rats with both incision and excision wound were made by cutting a skin from the dorsal abdomen region. The powdered plant of *E nivulia* were prepared as an ointment of two constrations (5, 10% w/w) and they used Framycetin sulphate (1 % w/w in Simple ointment) as a control refrance. Wound healing evalusted by measuring contraction rate of wound and regeneration of tissues at the site of wound.The results showed *E. nivulia* extract posses a significant wound healing ability when compared to control.They concluded that the wound healing activity is due to the presence of its active principles, which accelerate the healing process and confer tensile strength to the healed wound(S. Gopi Krishnan et al., 2019). S.Badgujar et al. reported that the fraction taken from the centrifuge of latex of *E. nivulia* enhanced the rate of wound contraction and period of epithelization in mice. The area of wound that treated with latex was reduced by 93 to 98 percent in compared to control group (90 percent) on the day 18(SB et al., 2009).

Euphorbia helioscopia

E. helioscopia is known as sun spurge(Webster, 1994).It is used in the treatment of various ailments like warts cure,skin diseases, intestinal parasites, migraine, gonorrhea(Webster, 1994, Kinghorn and Evans, 1975). N Jabeen et al. study the wound healing activity of both ethanol and aqueous extracts of *E. helioscopia* in wound rats with incision, excision and dead space models in compare with refrance drugs (1% w/w nitrofurazone gel). The wound healing was study by evaluate the epithelialisation, wound contraction, skin breaking strength, tissue granulation, hydroxylproline contents. The results showed that in the excision wound model, the animals treated with the ethanol extract produced faster epithelialisation (12.2 ± 0.5 mm 2) than those treated with the aqueous extract (16.5 ± 0.3 mm2),while the positive control produced an epithelialisation area of 11.2 ± 0.4 mm2. In the incision wound model, both ethanol and aqueous extracts treated group showed an increase in breaking strength (383.7 ± 3.6 g), (348.1 ± 3.2 g) respectively, as compared to the control (235.4 ± 2.8 g). In the dead space wound model, the ethanol extract treated animals showed a more significant rise in dry weight of granulation tissue (168.5 ± 0.6 mg/kg) as compared to the aqueous extract and control group(Jabeen et al., 2008).

CONCLUSION:

Most of these medicinal plants and natural products traditionally used for the treatment and management of various types of Skin diseases and wounds. These euphorbia plants Which have wound healing activity are usually sperad in

tropical and sub-tropical region. Wound healing properties of these selected plants assessed and evaluated through various in vitro and in vivo model studies, including the wound contraction, tensile strength, hydroxyproline content assay and histological investigations .The main constituents of Euphorbia plants which played the vital role in the wound healing process are flavonoids. Tannins, sterols and Polyphenols, saponins and Tri-terpenoids also asses wound healing process through several forms. At the same time these components reportedly promote wound healing by different pharmacological activity like mopping of reactive oxygen species from wounded tissues, inhibition / cidal effects against infections that delay wound healing and anti-inflammatory activities .These Euphorbia plants could be considered as Promising wound healing drugs. Further pharmacological and clinical investigations are recommended for exploring safety, exact mechanisms, and efficacy of these herbal remedies.

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