International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 18s, 2025
https://theaspd.com/index.php

Wound Healing Activity Of Different Extracts Of Some Indian Medicinal Plants In Some Animal Models

Dinesh Shakya[1*], Namrata Singh [2]
[1]PhD Research Scholar, Faculty of Pharmacy, Oriental University, Indore, Madhya Pradesh, India
[2]Faculty of Pharmacy, Oriental University, Indore, Madhya Pradesh, India
Correspondence Email Id- shakyadinesh164@gmail.com

Abstract
The advance oxidation protein products are markers of oxidative stress and protein glycation and mediators of oxidation of super oxide and plasma proteins. AOPP and neopterin are responsible for delayed macrophage activation and phagocytosis, which are the part of first phase of wound healing. The ethanolic and petroleum ether extracts were evaluated for wound healing activity in normal rats. The ethanolic extract showed highest significant wound healing activity than the other extracts by promotion of various biochemical factors in non treated rats. In wound healing study of ethanolic extract; the excision wound model was created to study the healing of wounds in terms of epithelialization, wound area and wound closure measurement. The ethanolic extract showed faster scar falling and epithelialization as compare to control non -treated normal rats. The Epithelialization represents the completion of remodelling and maturation phase and is the sign of complete healing of wound. The decrease in wound area resembles increased % of wound closure in treated rats. The faster wound closure is occurred only in condition of rapid proliferation of granuloma tissues.
In dead space wound healing model we studied inflammatory and proliferation phase of wound healing. The weight of wet granulation tissue express the inflammatory phase while the weight of dry granulation tissue with hydroxyproline, collagen and elastin represents the proliferation of granuloma tissue. The ethanolic extract treated rats showed increased weight of wet and dry granulation tissue at site of wound.
Keywords- *Wound Healing Activity, Different Extracts, Indian Medicinal Plants, Animal Models, Acacia arabica and Butea monosperma*

1. INTRODUCTION

The skin has the biggest surface area of any organ in the human body. Internal tissuesare protected by it from mechanical injury, microbial infection, UV light, temperaturevariations, and chemicals. Skin acts as a protective barrier between the body and the outside world, protecting it from physical harm, infections, and fluid loss, as well as having immunological activities that aid in the maintenance of hemostasis. (Maghraby *et al.*, 2008) Damage or disturbance to the normal integrity of anatomical structure and function is defined as a wound. This damage can range from a basic collapse of the skin's epithelial integrity to a deeper disintegration of subcutaneous tissue, causing damage to tendons, muscles, arteries, nerves, organs, and even bone structure. Wounds continue to be a difficult clinical problem in the health-care system, producing morbidity and mortality worldwide due to early and late consequences. Much study has concentrated on understanding the physiology of wound healing, with an emphasis on innovative therapeutic techniques and the development of wound management technology, in an effort to lessen the wound burden (Lemberger AP, 1973) Wounds develop as a result of pathological processes that begin either outside or inwardly within the organ in question. They can be the outcome of a disease process or have an accidental or intentional a etiology. Wound creation, regardless of the origin or form, destroys the tissue and changes the local environment within it.Bleeding, vascular constriction with coagulation and activation of an inflammatory response are all physiological responses to the noxious stimulus (Eswaraiah *et al.*, 2014). A large number of plants are used by folklore traditions in India for treatment of cuts, wounds and burns. The drugs selected for this work were *Acacia arabica* and *Butea monosperma*. These two important herbs are reported to have significant antibacterial, immune modulatory and anti-inflammatory activities which are complementary to wound healing process. The growing popularity of natural and herbal medications,

easy availability of raw materials, cost effectiveness and the paucity of reported adverse reaction, prompted us to formulate a polyherbal topical preparation and assess its wound healing ability (Robson *et al.*, 2001). In the absence of any scientific evidence for the wound healing activity of individual plants and the formulation of their active extracts an efforts were taken to study the effect of *Acacia arabica* and *Butea monosperma* for wound healing activity.

2. MATERIAL & METHODS

Plant Materials Collections

As per facts, references received from literature survey, the bark of *Acacia arabica* were purchased from local market and bark of *Butea monosperma* were collected from local area for investigational study.

Shading, drying and grinding:

The bark of *Acacia arabica* and bark of *Butea monosperma* dried under shade for 15 days. The dried bark was grinded under mechanical grinder machine to prepare cores powder, for extractions (Erim *et al.*, 2012).

Extraction of plant materials

The dried bark of *Acacia arabica* and bark of *Butea monosperma* were extracted by successive solvent extraction method with the help of soxhlet apparatus. The plant material first extracted with petroleum ether, chloroform, ethanol and water (Erim *et al.*, 2012).

Determination of percentage yield

The percentage yield of extract was calculated by using following formula: -

$$\text{Percentage yield} = \frac{\text{Weight of Extract}}{\text{Weight of powder drug Taken}} \times 100$$

Qualitative chemical examination

Preliminary Phytochemical analysis of different extracts was carried out by reported methods in Kokate & Khandelwal for the presence of different active phytoconstituents (Kokate & Purohit 2010).

Procurement and selection of animals

Wistar albino rats of either sex weighing between 100–150 gm of either sex were obtained from central animal house of our Institution. The animals were stabilized for 1 week; they were maintained in standard condition at room temp; normal light dark cycle. They had been given standard pellet diet and water *ad-libitum* throughout the course of the study. The animals were handled gently to avoid giving them too much stress, which could result in an increased adrenal output.

2.1. WOUND HEALING ACTIVITY OF DIFFERENT EXTRACTS

Excision wound healing activity in albino rats

Excision wounds were used for the study of rate of contraction of wound and epithelization; all wounds were of full-thickness type extending up to the adipose tissue. Animals were anaesthetized with slight vapour inhalation of di-ethyl ether and the back side of each rat was shaved. Excision wounds sized 300 mm^2 and 2 mm depth were made by cutting out piece of skin from the shaven area. The entire wound was left open. Animals were closely observed for any infection and those which showed any sign of infection were separated, excluded from study and replaced. The treatment was done topically in all the groups. The extract of both plants were applied at a dose of 200 and 400 mg/kg/day for 15 days. Wound areas were measured on days 1, 4, 8 and 15 for all groups, using a transparency sheet and a permanent marker. Recording of wound areas were measured on graph paper.The day of scar falling, after wounding without any residual raw wound was considered as the day of epitheliazation (Welch *et al.*, 1990).

Treatment Groups: For *Acacia arabica* different bark extracts treatment

1. **Group I:** Normal Wound Control; rats treated by 0.5% Sodium CMC orally.
2. **Group II:** Wounded rats orally treated by Pet ether extract in a dose of 200 mg/kg
3. **Group III:** Wounded rats orally treated by Pet ether extract in a dose of 400 mg/kg
4. **Group IV:** Wounded rats orally treated by Chloroform extract in a dose of 200 mg/kg
5. **Group V:** Wounded rats orally treated by Chloroform extract in a dose of 400 mg/kg

6. **Group VI:** Wounded rats orally treated by Ethanolic extract in a dose of 200 mg/kg
7. **Group VII:** Wounded rats orally treated by Ethanolic extract in a dose of 400 mg/kg
8. **Group VIII:** Wounded rats orally treated by Water extract in a dose of 200 mg/kg
9. **Group IX:** Wounded rats orally treated by Water extract in a dose of 400 mg/kg
10. **Group X:** Wounded rats topically treated by 5% Povidone ointment

Treatment Groups: For *Butea monosperma* different bark extracts treatment

1. **Group I:** Normal Wound Control; rats treated by 0.5% Sodium CMC orally.
2. **Group II:** Wounded rats orally treated by Pet ether extract in a dose of 200 mg/kg
3. **Group III:** Wounded rats orally treated by Pet ether extract in a dose of 400 mg/kg
4. **Group IV:** Wounded rats orally treated by Chloroform extract in a dose of 200 mg/kg
5. **Group V:** Wounded rats orally treated by Chloroform extract in a dose of 400 mg/kg
6. **Group VI:** Wounded rats orally treated by Ethanolic extract in a dose of 200 mg/kg
7. **Group VII:** Wounded rats orally treated by Ethanolic extract in a dose of 400 mg/kg
8. **Group VIII:** Wounded rats orally treated by Water extract in a dose of 200 mg/kg
9. **Group IX:** Wounded rats orally treated by Water extract in a dose of 400 mg/kg
10. **Group X:** Wounded rats topically treated by 5% Povidone ointment

Incision wound healing activity in normal rats:

Animals were anaesthetized with slight vapour inhalation of di-ethyl ether and the back side of each rat was shaved. A longitudinal paravertebral incision of six centimeters in length was made through the skin and cutaneous muscle on the back in anesthetized rats. After the incision, surgical sutures were applied at intervals of one centimeter. The wounds were left undressed and oral treatment was started. The sutures were removed on the 8th post wound day and the treatment was continued. The skin-breaking strength was measured on the 11th day by tensiometer (Trengove *et al.*, 1999).

Dead space wound healing activity in normal rats

Animals were anaesthetized with slight vapour inhalation of di-ethyl ether and the back side of each rat was shaved. Dead space wounds were inflicted by implanting sterile cotton pellets (10 mg each), one on left side in the groin and axilla on the ventral surface of each rat.[88] on the 10^{th} post-wounding day, the granulation tissue formed on the implanted cotton pellets was carefully removed under anaesthesia. After noting the weight of the granulation tissue, the tissue was dried at 60°C for 12 hr, and the dry granulation tissue weight was recorded. This dried tissue was further used to estimate hydroxyproline, collagen and elastin level in skin of normal rats (Akihisa *et al.*, 1996).

2.3. Biophysical and biochemical examinations in wound healing

Measurement of wound area

The wound area was measured with the help of graph paper. The wound area was traced on a transparent sheet of plastic and it kept on a graph paper for counting of no of small boxes in each traced area (1 Box = $1mm^2$).

Measurement of % wound closure

The % wound closure as calculated with the help of formula.

$$\% \text{ Wound closure} = \frac{(\text{Initial wound area} - \text{Final wound area})}{\text{Initial wound area}} \times 100$$

Day of epithelization

The day on which the scar was fall down from wound site considered as day of epithelization.

Measurement of tensile strength

The tensile strength was measured with the help of tensiometer. The tensiometer is used to measure the strength of wound or skin breaking weight. Two hooks of tension meter were tie or fixed either side of skin where incision was made. One side hook was fixed and other side hook was attached with a balance pan on with one empty bottle is placed. As we started to add water in bottle the weight of water pulled the hook followed with skin of wounded area. The weight of water at which skin of wounded area was broken considered as weight of wound breaking strength or tensile strength in gm/mm^2 (Jorge *et al.*, 2008).

Wet granulation tissue weight

The cotton inserted into dead space pocket of dead space wound model, when removed after completion of experiment and weighed. The weight of this cotton was considered as wet weight of granulation tissue (mg/100 gm of Rat).

Dry weight of granulation tissue

After measurement of wet weight of granulation tissue, the wet tissue was dried at 90˚C for 6 hrs. The weight of tissue after drying was considered as dry weight of granulation tissue (mg/100 gm of Rat) (Jorge *et al.*, 2008).

Estimation of hydroxyproline

The dried tissue after dry granulation weight kept in 6N HCl for 12 hrs at 120˚C. The hydroxyproline (A constituent amino acid of collagen and elastin) was extracted out from tissue and measured by following procedure.

1. Aliquots of standard hydroxyproline (2-20µg) prepared from stock solution and test samples containing hydroxyproline under 10µg/mL were mixed gently with sodium hydroxide (2N final concentration) in a total volume of 50 µL.
2. The sample was hydrolyzed by autoclaving at 120˚C for 20 min.
3. 450 µL of chloramines-T was added to the hydrolyzed, mixed gently, and the oxidation was allowed to proceed for 25 min at room temperature.
4. 500 µL of Ehrlich's aldehyde reagent was added to each sample, mixed gently and the chromophore was developed by incubating the samples at 65˚C for 20 min.
5. Absorbance of each sample was read at 550nm using a spectrophotometer to find out concentration of hydroxyproline.

Estimation of collagen content

Hydroxyproline is basic constituent of collagen. The content of collagen was calculated by using amount of hydroxyproline in following formula; (Jorge *et al.*, 2008).

% Collage Content = Weight of Hydroxyproline in tissue x 7.46 x 100

3. RESULTS & DISCUSSION

Determination of percentage yield of *Acacia arabica*

The % yield of petroleum ether, chloroform, ethanol and water extracts of dried bark of *Acacia arabica* was found 10.11, 4.45, 7.53, 8.50 % respectively (Table).

Table No. 1: % Yield of different extracts of *Acacia arabica*

S. No	Treatment	% Yield	Characteristics
1	Petroleum ether extracts	10.11%	Sticky & dark brown in color
2	Chloroform, Extract	4.45%	Sticky & dark brown in color
3	Ethanol Extract	7.53%	White in color
4	Water Extract	8.50%	Sticky & dark green color

Determination of percentage yield of bark of *Butea monosperma*

The % yield of petroleum ether, chloroform, ethanol and water extracts of dried bark of *Butea monosperma* was found 9.15, 6.24, 8.55, 4.58 % respectively (Table).

Table No. 2: % Yield of different extracts of bark of *Butea monosperma*

S. No	Treatment	% Yield	Characteristics
1	petroleum ether extracts	9.15%	Dark brown in color
2	Chloroform, Extract	8.55%	Sticky brown in color
3	Ethanol Extract	4.58 %	Brownish in color
4	Water Extract	8.50%	Sticky and White in color

Qualitative Chemical Examination of *Acacia arabica*

On qualitative phytochemical examination of different extracts of *Acacia arabica* bark the test for carbohydrate was found positive. Proteins were found only in petroleum extract. The steroidal test was negative only in ethanolic extract but positive in all other extracts. Glycosides were present in chloroform and water extract. All extract were given positive test for presence of alkaloids except petroleum ether. Test for flavonoids was found positive in ethanolic and chloroform extract. The test of phenolic and tannin compounds was positive in all extracts except petroleum ether. The ethanolic extract of showed presence of high amount of phenolics and tannin compounds (Table)

Table No. 3: Presence of phytocompounds in different extracts

S. No.	Name of Phytochemicals	Pet. Ether Extract	Chloroform Extract	Ethanol Extract	Water Extract
1	Test for carbohydrates	+	+	+	+
2	Test for Proteins	-	-	+	-
3	Test for steroids	-	+	+	++
4	Test for Glycosides	-	++	-	++
5	Test for Alkaloids	+	+	+	+
6	Test for flavonoids	++	++	-	+
7	Test for phenolic & tannin compounds	+++	++	-	++

Qualitative Chemical Examination of *Butea monosperma*

On qualitative phytochemical examination of different extracts of *Butea monosperma* bark the test for carbohydrate was found positive. Proteins were found only in petroleum extract. The steroidal test was negative only in ethanolic extract but positive in all other extracts. Glycosides were present in chloroform and water extract. All extract were given positive test for presence of alkaloids except petroleum ether. Test for flavonoids was found positive in ethanolic and chloroform extract. The test of phenolic and tannin compounds was positive in all extracts except petroleum ether. The ethanolic extract of showed presence of high amount of phenolics and tannin compounds (Table)

Table 4: Presence of phytocompounds in different extracts

S. No.	Name of Phytochemicals	Pet. Ether Extract	Chloroform Extract	Ethanol Extract	Water Extract
1	Test for carbohydrates	+	+	+	+

2	Test for Proteins	-	-	+	-
3	Test for steroids	-	+	+	++
4	Test for Glycosides	-	++	-	++
5	Test for Alkaloids	+	+	+	+
6	Test for flavonoids	++	++	-	+
7	Test for phenolic & tannin compounds	+++	++	-	++

WOUND HEALING ACTIVITY OF DIFFERENT EXTRACTS

Effect of dried extracts of *Acacia arabica* on Excision wound parameters

As per figures, In Excision wound model the seeds extract treated rats showed significant healing of wounds as compared to non treated rats. In Extract treated groups; ethanolic extract of both plants treated rats showed highest wound closure 96.44% after 11 days of continuous treatment with extract ointment, which was more than 79.86% of normal control group respectively. The chloroform extract and pet ether extract treated groups also exhibited significant increase in wound closure more than both control groups. The Table demonstrates that the wound area of ethanolic extract treated rats was measured about 10.33 mm^2 which was very much less than non treated normal (50.33 mm^2) rats. In other treatment groups the chloroform and methanol extract treated rats also showed significant decrease in wound area upto 21.67 and 27.67 mm^2 respectively. Ethanolic extract treated group the day of scar falling i.e. final epithelization was observed on 17^{th} day of wounding which was more than the normal control and other extract treated groups. The chloroform and methanol extract treated groups also showed faster scar falling as compared to non treated rats.

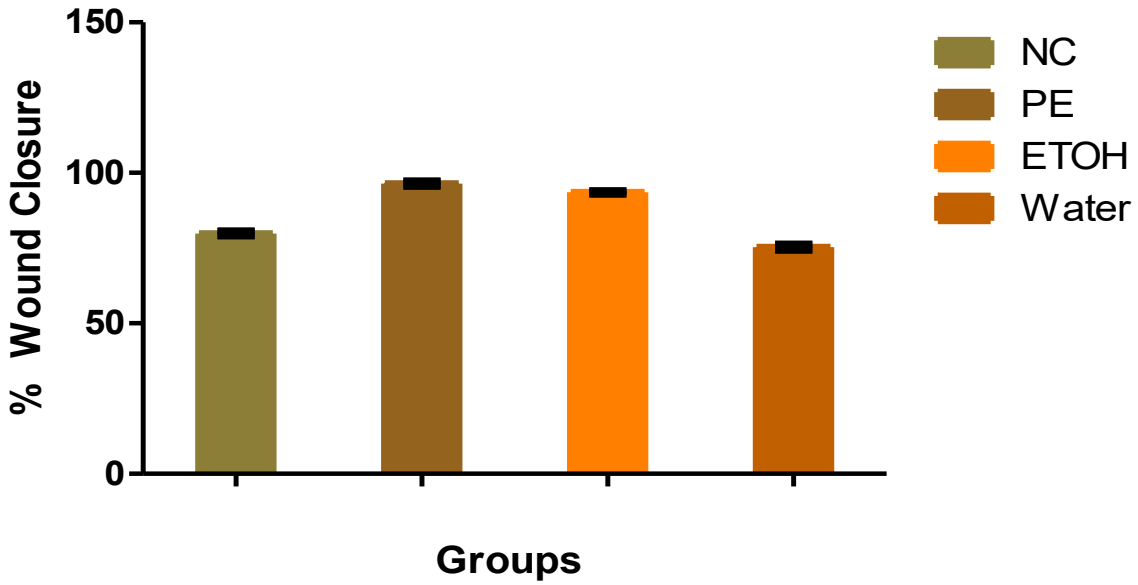

Figure No.1: Effect of Different extracts on wound closure

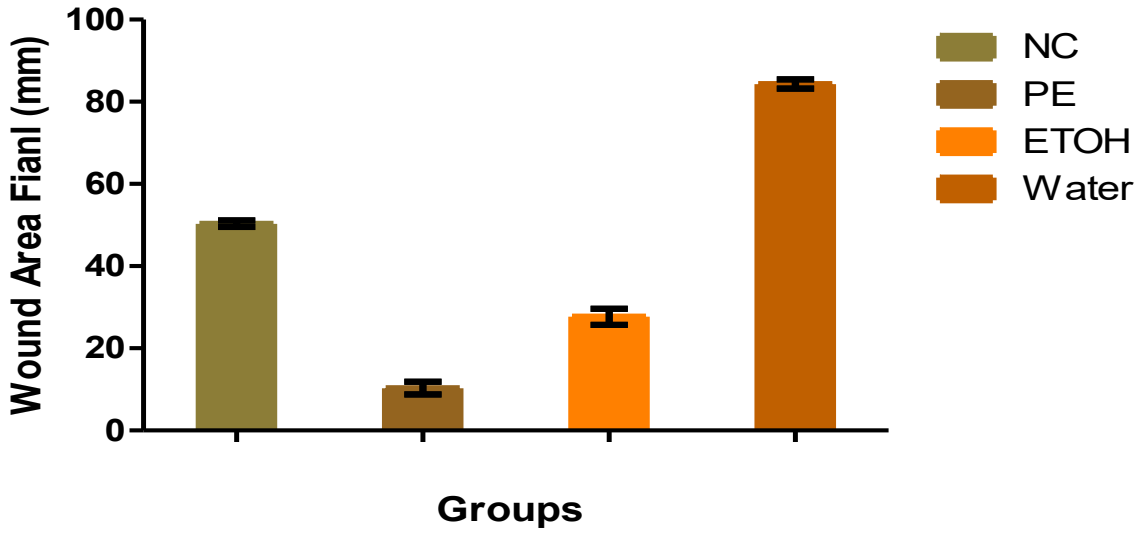

Figure No.2: Effect of Different extracts on wound area final

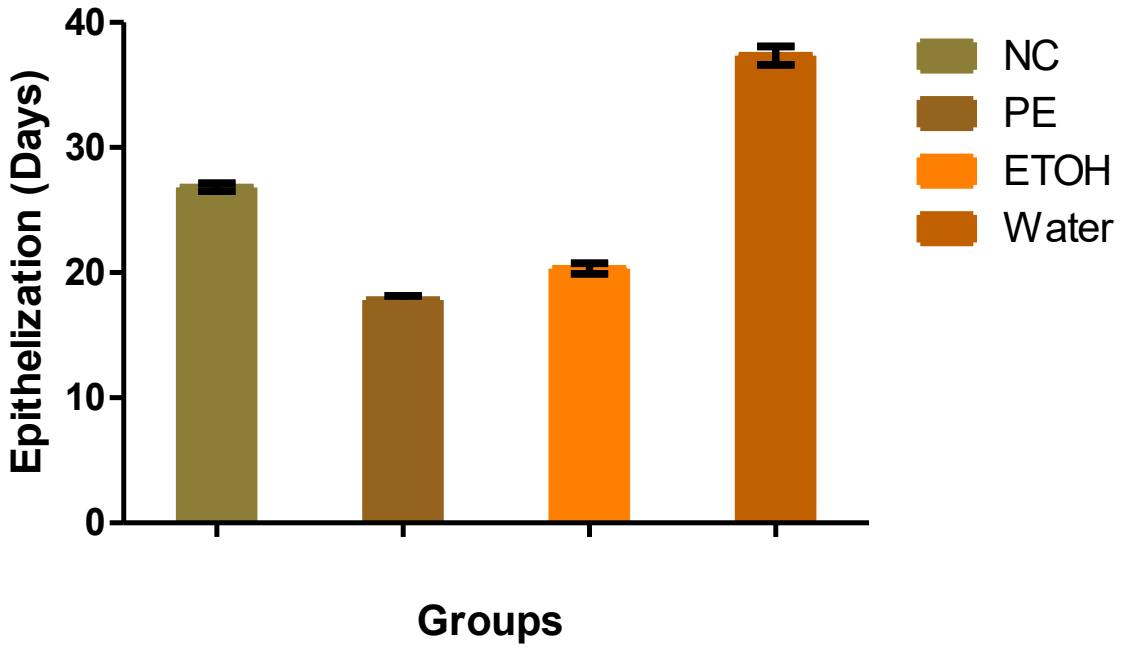

Figure No.3: Effect of Different extracts on Epithialization

Data are expressed as Mean ± SEM and analyzed statistically by One way ANOVA followed by Dunnett's Multiple Comparison Test, using Graph Pad Prism Software trial version. IN Dunnett's Multiple Comparison Test, Group NC was compared with treated groups. P value considered as P<0.05 Significant (*), P<0.01 Very Significant (**), P<0.001 Highly Significant (***).

Effect of *Butea monosperma* bark extracts on Excision wound parameters

Ethanolic extract treated group the day of scar falling i.e. final epithelization was observed on 17th day of wounding which was more than the normal control and other extract treated groups.

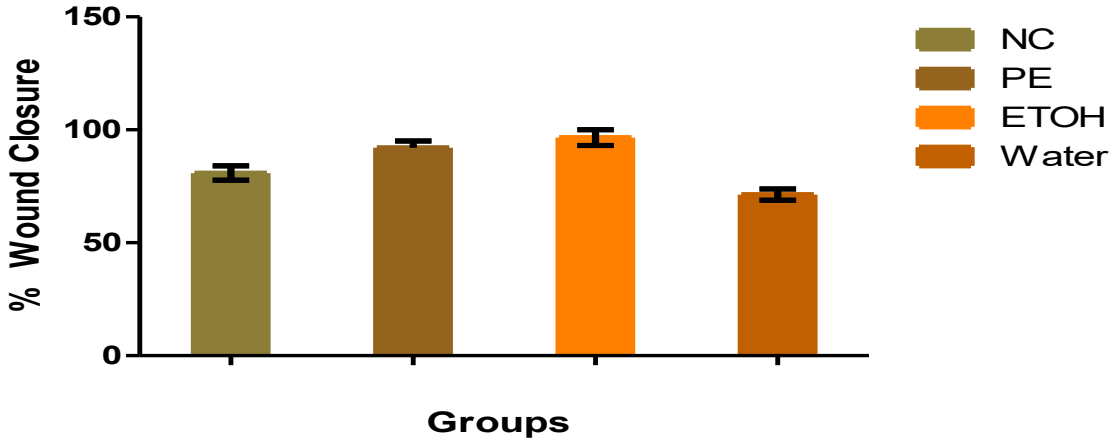

Figure No.4: Effect of Different extracts on % Wound Closure

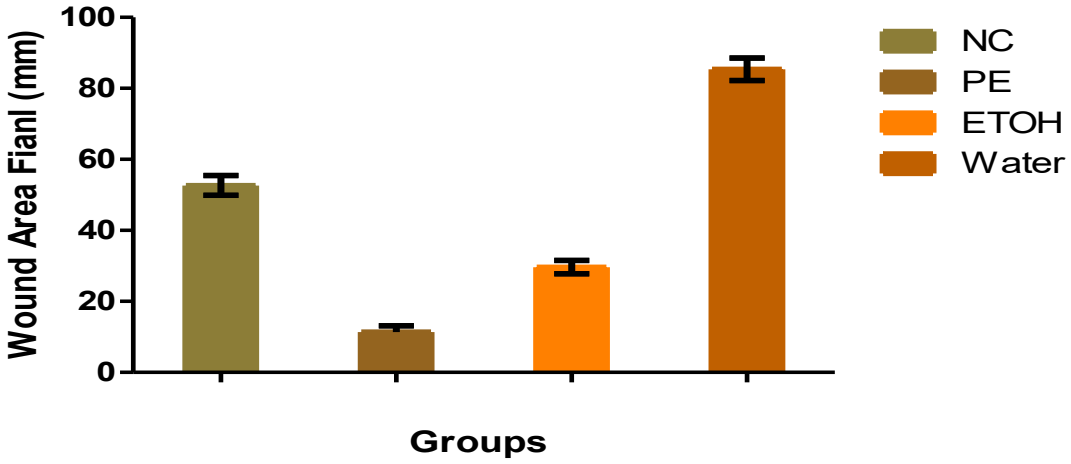

Figure No.5: Effect of Different extracts on Wound Area Final

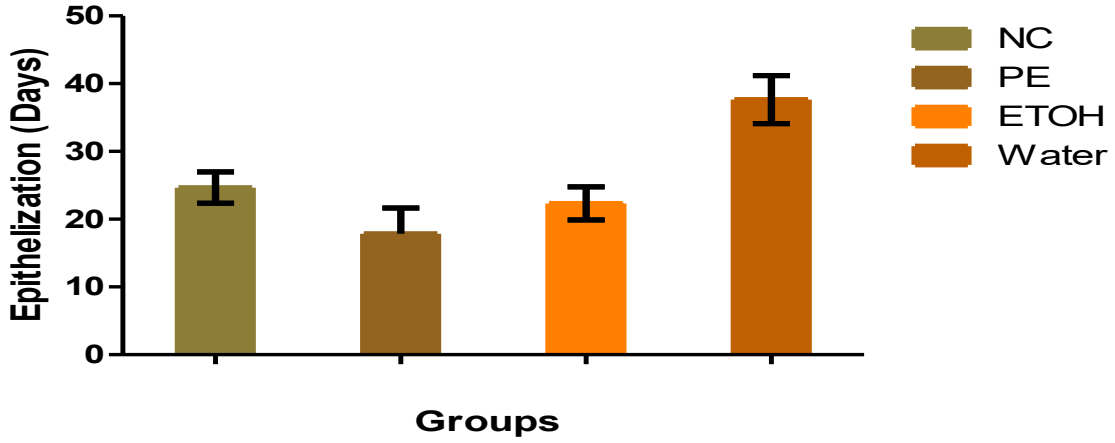

Figure No.6: Effect of Different extracts on Epithialization

Effect of dried bark extracts on Incision and Dead Space wound parameters

According to results expressed in Table; in Incision wound model among the extract treated rats ethanolic extract of both plants treated rats showed highest tensile strength 311.4 gm/mm^2 during examination of wound breaking as compared to animals of normal (241.5 gm/mm^2) control groups. While in other

extract treated groups except petroleum ether treated rats, chloroform, Methanol and acetone extract treated rats showed more wound breaking strength 268.4, 254.4 and 218.9 gm/mm^2 respectively.
In dead space wound model as per Table; the ethanolic extract treated rats exhibited higher weight of wet (337.3 mg) and dry (102.5 mg) granulation tissue as compared to weight of wet (233.2 mg) and dry (64.83 mg) granulation tissue in rats of normal control group.
During comparison for weight of hydroxylproline, % of collagen and elastin tissue the ethanolic extract treated rats expressed higher amount of hydroxyproline (8.595µg/ml), collagen (64.12%) and elastin (373.0 %) as compared to animals of non treated normal control groups 5.5 µg/ml, 41.05 % and 238.8 % respectively. The other extract treated rats also possesses higher amount of hydroxylproline, % of collagen and elastin in granulation tissue than rats of normal control group.

Table No. 5: Effect of *Acacia arabica* bark extracts on Incision and Dead Space wound parameters

Groups Parameters	Normal Control	Pet. Ether Extract	Chloroform Extract	Ethanolic Extract	Water Extract
Tensile Strength (gm/mm^2)	241.5± 3.279	311.4± 2.856 ***	254.4± 3.410 ***	224.9± 3.577 ***	268.4± 2.732 ***
Wet Granulation Tissue Wt. (mg)	233.2± 3.176	337.3± 1.606 ***	216.0± 2.176 ***	191.7± 2.044 ***	304.3± 1.687 ***
Dry Granulation Tissue Wt. (mg)	64.83± 1.537	102.5± 2.643 ***	71.67± 0.8819 ***	45.67± 1.667 ***	79.83± 1.352 ***
Hydroxy-proline (µg/ml)	5.503 ± 0.1093	8.595± 0.1056 ***	6.253± 0.0605 ***	4.457± 0.088 ***	7.445± 0.0833 ***
% Collagen	41.05± 0.8155	64.12± 0.7880 ***	46.65± 0.4520 ***	34.14± 0.7273 ***	55.54± 0.6217 ***

Table No. 5: Effect of *Butea monosperma* bark extracts on Incision and Dead Space wound parameters

Groups Parameters	Normal Control	Pet. Ether Extract	Chloroform Extract	Ethanolic Extract	Water Extract
Tensile Strength (gm/mm^2)	241.52± 3.22	313.45± 2.33 ***	254.33± 3.55 ***	226.33± 3.11 ***	266.44± 2.23 ***
Wet Granulation Tissue Wt. (mg)	233.22± 3.76	337.35± 3.66 ***	217.44± 2.176 ***	193.78± 2.44 ***	305.66± 3.87 ***
Dry Granulation Tissue Wt. (mg)	64.86± 1.57	104.54± 2.63 ***	71.87± 2.19 ***	45.55± 1.87 ***	78.53± 1.32 ***
Hydroxy-proline (µg/ml)	5.53 ± 0.13	8.59± 0.16 ***	6.25± 0.55 ***	4.47± 0.58 ***	7.45± 0.83 ***

% **Collagen**	41.33± 2.85	64.34± 2.70 ***	46.22± 1.52 ***	34.44± 2.73 ***	55.78± 3.21 ***

The main aim of life for every human being is to live with joy and happiness. The diseases and injuries create many problems in front of population against survival. Physicochemical stress in the body produces several complications in patient including delayed healing of wound, cardiovascular diseases, defect in vision, renal disorders, neuronal disorders and many more. Immunocompromised patients should have more care against any injury or wound, because the wound or injuries are difficult to heal and take more time to come at normal physiological state (Reddy *et al.*, 2008). In chronic hypoxic state, the metabolites of proteins, glucose and lipid metabolism generate oxidative free radicals; which upon interaction with other biomolecules, create a complex structure called advance metabolic protein end products. These false protein again react with other biomolecules i.e. proteins, hormones, enzymes, growth factors, receptors and other cellular components. There are several drugs available in modern system of medicine to treat wound healing and its complications but all synthetic modern medicines available in market having verity of side effects and slow action. When we review the natural and herbal (Ayurvedic) system of medicine, the available medication is more reliable and effective in complete treatment of wound healing, hypertension, heart disease, diabetes, metabolism and liver disorders and many other problems of body (Shukla *et al.*, 1999).

In Indian system of medicine, the *Acacia arabica* and *Butea monosperma* is from some popular herbs used in treatment of several diseases including infections, poisonous diseases; late wound healing, GIT disorders, digestive disorders, diabetes, constipation, immunity and many others. Numbers of investigators have worked on several properties of this plant including their antimicrobial, maintenance of circulation, hepatoprotective, anti ulcer and antioxidant etc. On the basis of literature reviewed, it was decided to investigate wound healing property of bark of *Acacia arabica* and *Butea monosperma* in normal rats (Nehete *et al.*, 2015). In incision wound model all extracts were administered orally at a dose of 200 mg/kg body weight for 14 days. At the end of study tensile strength (Skin breaking strength) was measured with the help of tensiometer. In Dead Space wound model all extracts were administered orally at a dose of 200 mg/kg body weight for 14 days. At the end of treatment the wet and dry weight of granulation tissue, hydroxyproline content with % collagen level also estimated in blood of rats of dead space wound model. Among all extracts ethanolic extract of bark of *Acacia arabica* and *Butea monosperma* were found to be most effective in management of delayed wound healing (Xu-Kun Deng *et al.*, 2006). The acute (Oral and Dermal) toxicity studies, excision, incision and dead space wound model were implicated for wound healing activity of ethanolic extract of *Acacia arabica* and *Butea monosperma* with all biophysical and biochemical parameter estimation same described above for examination of extract (Wu Yin *et al.*, 2003).

CONCLUSION

On the basis of above investigations, it is concluded that the ethanolic extract of bark of *Acacia arabica* and *Butea monosperma* have effective role in treatment of delayed wound healing in normal albino rats. The herbal formulations made by above said extracts could be more beneficial for society, and further study related with isolation of potent chemical compounds and responsible biological quantitative confirmation from bark of *Acacia arabica* and *Butea monosperma* could meet in the form of treatment for physical or chemical injury complications especially for wound healing complications in patients.

REFERENCES

1. Maghraby GM, Barry BW, Williams AC. Liposomes and skin: From drug delivery to model membranes. European Journal of Pharmaceutical Sciences 2008; 34(4): 203-222.
2. Lemberger AP. A Hand Book of Non Prescription Drug 1973; 5th ed.: American Pharmaceutical Association, Washington, 14: 161.

3. Eswaraiah S, Swetha K, Lohita M, Jaya Preethi P, Priyanka B, Reddy KK. Emulgel: Review on Novel Approach to Topical Drug Delivery. Asian Journal of Pharmaceutical Research 2014; 4(1): 04-11.
4. Robson MC, Steed DL, Franz MG. Wound healing: biologic features and approaches to maximize healing trajectories. Current Problems in Surgery 2001; 38: 72 – 140.
5. Erim G, Ays_egul K, Kasim C, Murat T, Habib E, Lokman K, Yasemin A, Umit A. Topical effects of nebivolol on wounds in diabetic rats. European Journal of Pharmaceutical Sciences 2012; 47: 451–455
6. Welch MP, Odland GF, Clark RA. Temporal relationships of F-actin bundle formation, collagen and fibronectin matrix assembly, and fibronectin receptor expression to wound contraction. Journal of Cell Biology 1990; 110: 133-145.
7. Trengove NJ, Stacey MC, MacAuley S, Bennett N, Gibson J, Burslem F, Murphy G, Schultz G. Analysis of the acute and chronic wound environments: the role of proteases and their inhibitors. Wound Repair and Regeneration 1999; 7: 442-452.
8. Akihisa T, Yasukawa K, Oinuma H. Triterpene alcohols from the flowers of compositae and their anti-inflammmatory effects. Phytochemistry 1996; 43: 1255-1260.
9. Jorge MP, Madjarof C, Ruiz ALTG, Fernandes AT, Rodrigues RAF, Sousa IMO, Foglio MA, Carvalho JE. Evaluation of wound healing properties of *Arrabidaea chica Verlot* extract. Journal of Ethnopharmacology 2008; 118: 361-366.
10. Reddy BS, Reddy RKK, Naidu VGM, Diwan PV. Evaluation of antimicrobial, antioxidant and wound healing potentials of *Holoptelea integrifolia.* Journal of Ethnopharmacology 2008; 115: 249-256.
11. Shukla A, Rasik AM, Jain GK, Shankar R, Kulshrestha DK, Dhawan BN. *In vitro* and *in vivo* wound healing activity of asiaticoside isolated from *Centella asiatica*. Journal of Ethnopharmacology1999; 65: 1-11.
12. Nehete M, Nipanikar S, Kanjilal A, Kanjilal S, Tatke P. Comparative efficacy of two polyherbal creams with framycetin cream in treating fresh wounds. European journal of pharmaceutical and medical research. 2015; 2(5): 1047-1057.
13. Kokate C K, Purohit A P, Gokhale S B, Pharmacognosy vol I & II, 45th edition, June 2010, Nirali publication, Pune-5, p 3.18-3.21, 3.44-3.46, 1.133-1.136.
14. Wu Yin,Tian-Shan Wang, Fang-Zhou Yin and Bao-Chang Cai, Analgesic and anti-inflammatory properties of brucine and brucine-N-oxide extracted from seeds of *Strychnos nux vomica* Journal of Ethanopharmacol 2003; 88:205-214.
15. Xu-Kun Deng, Wu Yin, Wei-Dong Li, Fang-Zhou Yin, Xiao-Yu Lu *et al.*, The anti-tumor effects of alkaloids from the seeds of *Strychnos nux- vomica* on HepG2 cells and its possible mechanism, *Journal of Ethnopharmacol*, 2006; 106(2): 179-186. 341