Wounds can occur due to any injury, disease state or insect bite or abrasions. Wound healing is a complex process that includes many phases and involves a number of inflammatory mediators wound can be classified as acute and chronic. Other than this wound can also be classified on the basis of layer of skin that gets damaged: Superficial wound, Partial thickness wound and Full thickness wound. Garlic (*Allium sativum*) has been used as food and also used for the treatment of many diseases, for healing of wounds etc. Garlic is perennial liliaceous herb with a bulb having organosulphur compounds like Diallyl disulphide, diallyl sulphide, diallyl trisulphide and sulphur dioxide others are allin, allicin, etc. Garlic having major properties includes anti-cancer, against cardiovascular disease, anti-oxidant, anti-microbial, in wound healing etc.

**Introduction**

Skin act as protective barrier for the body which protects the body from external environment. Epidermal layer of skin can be damaged due to injury that subsequently leads to the formation of the wound. Wounds can occur due to any injury, disease state or insect bite or abrasions. These are defined as the breakage in the regular continuity or integrity of tissue. Subsequent to the wound injury there is inflammation followed by infection in the wounded area. Invasion by various pathogenic microorganisms at the wounded tissue results in severe infection of the wounded surface. Anatomical and functional integrity of tissue get disrupted due to chronic wound infection. The humoral and cellular components of body play an active role in the pathogenesis of wound infection (Steven Percival, Keith Cutting).

The most commonly seen wounds in humans are the lower extremity wounds in diabetic patients, wounds following extensive necrosis followed by infection and the chronic wounds (Hermans, M.H.E. and T. Treadwell).

Wound healing is a complex process that includes many phases and involves a number of inflammatory mediators. Complex biochemical events such as inflammation, coagulation, homeostasis, proliferation and granulation tissue formation are involved in wound healing. These events are divided into three phases: inflammatory, proliferative and remodelling phase. But different endogenous and exogenous factors such as microbial infection on wound, poor blood supply to the wound area and nutritional deficiency such as vitamin C and Zinc results in delay in healing of wound (Thomas *et al.*, 2011).

On the basis of mechanism and duration of healing, wound can be classified as acute and chronic. Other than this wound can also be classified on the basis of layer of skin that gets damaged: Superficial wound, Partial thickness wound and Full thickness wound. Currently a wide range of topical antibiotics, antifungal and antiseptic drugs are used for the treatment of wound infections. Other than these new effective techniques such as tissue engineered growth technique, recombinant growth factors and silver dressings are also used nowadays for the treatment of wound infections. A number of cleansing solutions and gels are also used for rinsing and cleaning of wound such as sterile normal saline, sterile water, Povidone iodine, Poly-hexane biguanide and sodium hypochlorite (Benjamin A. Lipsky1,2 and Christopher Hoey).

Marketed antimicrobial drugs used for the treatment of wound infections are associated with various side effects like itching, redness of skin and blister formation. Resistant cases with the use of topical antibiotics and antifungal are also rising nowadays. This led to failure of antimicrobial therapy used to treat wound infection. Other than this major drawback associated with new advanced effective techniques such as recombinant growth factor, silver dressings is that these are very expensive (Tiwari and Jain, 2011).

Considering the limitations associated with the commercially available antibiotics and newer techniques, there is urgent need to develop as safer and cost-effective wound healing agent. Medicinal plants have been used from the ancient time for the treatment of various ailments. Large money has been invested by the pharmaceutical companies to isolate the essential Phyto-constituents from the medicinal plants to use them as efficacious medicinal and
A number of medicinal plants which contain alkaloids and flavonoids as chief chemical constituents can effectively enhance the wound healing process. Medicinal plants such as Neem, Aloe Vera, Tulsi are rich source of alkaloids and flavonoids, so such plants can strongly enhance the wound healing process.

The present review article summarizes the role of garlic on the wound healing process

Properties of garlic
(1) Anti-oxidant properties:

<table>
<thead>
<tr>
<th>Organosulphur compounds</th>
<th>Beneficial effects</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Garlic oil</td>
<td>Reduce toxicity of terbutylin</td>
<td>Liu and Xu (2007)</td>
</tr>
<tr>
<td>Aged garlic extract</td>
<td>Suppress the development of glycation end products and formation of glycation derived free radicals, Inhibit lipid peroxidation and oxidation of low-density lipoprotein (LDL)</td>
<td>Ahmad and Ahmad (2006)</td>
</tr>
<tr>
<td></td>
<td>Guard the tissue against nicotine induced oxidative disruption</td>
<td>Amagase et al. (2001), Lau(2006)</td>
</tr>
<tr>
<td>Aq. Garlic extract</td>
<td>Scavenges hydroxyl radicals</td>
<td>Augusti(1996)</td>
</tr>
<tr>
<td>Allicin</td>
<td>Decrease the liver damage caused by carbon tetra chloride</td>
<td>Prasad, Haxadal and Yu(1995), Fukao et al. (2004), (S.G. Santhosha, Prakash Jamuna, S.N. Prabhavathin)</td>
</tr>
<tr>
<td>Di-allyl tri-sulphate</td>
<td>Do not show scavenging activity</td>
<td></td>
</tr>
</tbody>
</table>

2,2-diphenyl-1-picrylhydrazyl (DDPH), a scavenging technique or method is used to identify the anti-oxidant property of raw garlic which shows a change in colour from violet to yellowish which indicates antioxidant property. However (HPLC) high performance liquid chromatography technique doesn’t give appropriate conclusion about presence of allicin (Rahman, M. M et al).

Aged extracts which obtained from the leaves, they show best anti-oxidant property, however flower bulblets express less or no activity. (Anna Capasso)

Polyphenol groups helps to fight against the oxidative stress which affect membranes, nucleic acid, celluler component etc. (Florinda Fratianni)

(Gaber El-Saber Batih)
(2) Anti-microbial activity

<table>
<thead>
<tr>
<th>Product</th>
<th>Compound</th>
<th>Cell lines</th>
<th>Major effect</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raw garlic</td>
<td>------</td>
<td>15 patients with H. pylori infection</td>
<td>Suppressing the Helicobacter pylori in the stomach</td>
<td>Zardast, M.; Namakin (Ao Shang)</td>
</tr>
</tbody>
</table>

1.) Table showing Different garlic compounds showing activity against microorganisms e.g., Penicillium expansum, Burkholderia cepacian, Staphylococcus aureus etc.

Garlic is a broad spectrum compound having antibacterial and anti-fungal property. (Fratianni, F.; Riccardi.). Different varieties of garlic “Rosato” and “Caposele” significantly inhibit the growth of microbes e.g., Rosato inhibit Penicillium citrinum and Aspergillus versicolor and Caposele have strong effect on inhibition of penicillium expansum (Fratianni, F.). Garlic oil also possess antibacterial properties to inhibit the growth of Staphylococcus aureus and Escherichia coli (Guo) (Ao Shang).

First man who purposes the attributes regarding antibacterial in case of garlic are Louis Pasteur in 1858 and exhibit the allicin as the main active constituent. (Block, 1992; Nagourney, 1998) (P. Avato, F. Tursi). Garlic contain 3 times sulphur compounds as similar as onions (Lawson) (N. Benkeblia). These compounds are high in reaction, volatile in nature, odour producing and lachrymatory (Block, Naganathan, Putman, & Zhao, 1992). (N. Benkeblia). The antibiotic activity of 1mg of llicin, which is S-methyl-L-cysteine has been equal to 15 IU of penicillin. s (Sivam, Lampe, Ulness, Swanzey, & Potter, 1997; Phay et al., 1999; Hsieh, Mau, & Huang, 2001;

Garlic oil also express antifungal properties by penetrating into cells and organelles, by disrupting the cell structure etc. Inhibit the groth of fungus e.g. Penicillium funiculosum etc. (Li, W.R.; Shi) (Ao Shang) Garlic extracts have shown strong activity against fungus and suppress the synthesis of mycotoxins e.g. aflatoxin of Aspergillus parasiticus. (Lawson L.D.,) (Serge Ankri) Pure allicin have large amount of anti- candida property with Minimum MIC concentration of 7μg/ml. (Hughes B.G.,) (Serge Ankri)

Ant-Fungal Activity test

1.) Anti-fungal activity test was performed under in vitro conditions, petri plate containing Yeast Glucose Chloramphenicol Agar) (Lattenzio, De Cicco, Di Venere) (N. Benkeblia)
2.) Essential oil extract was added to Yeast Glucose Chloramphenicol Agar
3.) For control test, add sterile water to YGCA media (50, 100, 200, 300 and 500 ml/l, vol/vol).
4.) Inoculate fungi in above petri plates in centre of 5mm of diameter of mycelial mass of cultivated test fungi
5.) Cut with sterile cork borer
6.) Incubate petri plates at 21°C in dark
7.) Stop the incubation when mycelial growth mass of petri plates almost filled the petri dish
8.) Diameter was Identified by averaging the radial growth of mycelial mass in two orthogonal directions. (N. Benkeblia)

Use of raw garlic is to suppress the growth of Helicobacter pylori in stomach of patient to protect it from H. pylori from infection. Extract of garlic possess activity against H. pylori which is the main reason for gastric ulcers. (Zardast, M.; Namakin) (Ao Shang). Different garlic compounds and their preparations possess wide spectrum anti- bacterial properties against gram negative and gram-positive bacteria involving Salmonella, Staphylococcus, Streptococcus etc. (Uchida Y., Takahashi T) (Serge Ankri)

In the recent studies it was observed that about 1 to 2 percent of garlic extract having anti-microbial activity. The main component of garlic S-methyl L-cysteine sulfoxide is enzymatically divided into methyl methanethiosulfinate, as same like allin is converted into allicin with the help of enzyme alliinase. MMTSO is a strong antimicrobial compound but as low as compared to allicin. (Small et al., 1947). (Kyu hang kyung)

(3) Prevention against cardiovascular disease

<table>
<thead>
<tr>
<th>Product</th>
<th>Compound</th>
<th>Possible mechanism</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aged black garlic extract</td>
<td>Polyphenols</td>
<td>Stimulating the production of NO</td>
<td>Takashima, M.;</td>
</tr>
<tr>
<td>Aged Garlic extract</td>
<td>S-1-propylenecysteine</td>
<td>----</td>
<td>Garcia-Villalon, A.L.;</td>
</tr>
<tr>
<td>Fermented garlic extract</td>
<td>---</td>
<td>Decreasing the expression of vascular endothelial cell adhesion molecule-1 and MMP9Increasing the expression of PKG and eNOS</td>
<td>Park, B.M.; Chun, H</td>
</tr>
<tr>
<td>Garlic</td>
<td>Alliin</td>
<td>----</td>
<td>Asdaq, S.M.; Inamdar, M.N</td>
</tr>
</tbody>
</table>
In the following tables Compounds showing different properties against CVS.

Cardiovascular disease is directly linked to increase in various factors such as increase in platelet aggregation, increase in cholesterol, increased in low density lipoprotein, etc. (Rahman K). Different preparations e.g. oil of steam distilled garlic, garlic powder and aged garlic extract used in CVS diseases in clinical trials (Banerjee SK, Mukherjee PK, Maulik SK) (Khalid Rahman and Gordon M. Lowe).

(4) Effect of garlic products on platelet aggregation

<table>
<thead>
<tr>
<th>Products</th>
<th>Duration</th>
<th>Effect</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Garlic oil</td>
<td>In vitro</td>
<td>Suppress platelet aggregation</td>
<td>Vanderhock et al., 1980</td>
</tr>
<tr>
<td>Garlic powder</td>
<td>Four weeks</td>
<td>Suppress PA</td>
<td>Kiesewetter et al., 1991</td>
</tr>
<tr>
<td>Aged garlic extract</td>
<td>Ten months</td>
<td>Suppress PA</td>
<td>Steiner and Lin, 1998</td>
</tr>
<tr>
<td>Dried garlic powder</td>
<td>Four weeks</td>
<td>No PA effect</td>
<td>Harenberg et al., 1988</td>
</tr>
<tr>
<td>Essential garlic oil</td>
<td>Ten days</td>
<td>No PA effect</td>
<td>Samson, 1982</td>
</tr>
<tr>
<td>Ether extract of garlic</td>
<td>Single dose</td>
<td>Increased coagulation time</td>
<td>Arora and Arora, 1981</td>
</tr>
</tbody>
</table>

Table shows the activity of garlic products on platelet aggregation

In vitro clinical trials shows that garlic extract improves circulation of blood and blood properties. (Moriguchi T, et al.). Garlic improves the fluidity of erythrocytes isolated from hypecholesterolemic rats (Kempaiah RK, Srinivasan K) (Khalid Rahman and Gordon M. Lowe).

Different activities shown by garlic e.g., Anti-hypertensive, Anti-Hyperlipidaemic, Anti-Platelet activity, Anti-Atherosclerotic activity.

(5) Prevention against cancer

Garlic is major medicinal plant that is also used for the treatment of atherosclerosis and their prevention. Garlic based preparations are also used as anti-atherosclerotic effects such as lowering plasma fibrinogen level etc (Campbell JH, Efendy JL, Smith NJ, et al) (El-Sabban F, Abouazra H).

Different activities shown by garlic e.g., Anti-hypertensive, Anti-Hyperlipidaemic, Anti-Platelet activity, Anti-Atherosclerotic activity.

(6) Organosulphur compounds with antineoplastic properties

<table>
<thead>
<tr>
<th>Compound</th>
<th>Cell type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ajoene</td>
<td>Lymphocytes, leukemic, colonic</td>
</tr>
<tr>
<td>Diallyl sulphide</td>
<td>Leukocyte, prostate</td>
</tr>
<tr>
<td>S-allyl cysteine</td>
<td>Melanoma, neuroblastoma</td>
</tr>
<tr>
<td>Diallyl disulphide</td>
<td>Lung, colonic, skin, prostate</td>
</tr>
<tr>
<td>Allicin</td>
<td>Lymphoid (Sigounas et al., 1997) (J. A. Milner)</td>
</tr>
</tbody>
</table>

NOC’s are biological and environmental indicator that may increase the chances of cancer in human body (Brown 1999; Ferguson 1999). Exposure of NOC may occur through the nasal route and through ingestion of the precursors (Lijinsky 1999) (J. A. Milner)

Frequent study in china reported that consumption of allium vegetables or garlic compounds decreases the chances of stomach cancer (Adetumbi, M. A) (Martha Thomson). Allium vegetables include garlic, onion, leeks, garlic stalks are used to treat stomach cancer (Holly L. Nicastro).
(7) Inhibition of tumour growth

Acc. To Pan XY, Li FO, et al., tested the effect of garlic extract and diallyl trisulphide on two human gastric cancer cell lines. In this trial, garlic extract and allyl disulphide were more potent as compared to fluorouracil and mitomycin C to treat cancerous cells (Pan XY, Li FQ, Yu ILI, Xie GF, Wang H, Zhao LY, Zhaog O) (Benjamin H.S. Lau).

S-allyl mercaptocysteine is water soluble organo sulphur compound having anti-oxidant property and suppress the cell growth and increase the apoptosis in cancer cell lines (Xiao J, Ching YP) (Maryam Miraghajani). SACMC is preferable for longer term treatment because SAMC has very less side effects like irritating (Tanaka S, Haruma K) (Maryam Miraghajani) and having no adverse effects and interaction with medication of aged garlic. (Macan H,) (Maryam Miraghajani).

(8) Possible Mechanism

Major group which shows the anti-neoplastic or anti-cancer effect are one is lipid soluble and another one is water soluble.

(9) Compounds showing different cancer’s mechanism

<table>
<thead>
<tr>
<th>Compound</th>
<th>Cancer type and mechanism</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ajoene</td>
<td>Leukaemia: Inhibit proliferation</td>
<td>Ahmed et al</td>
</tr>
<tr>
<td></td>
<td>Induce apoptosis by suppressing the G2 phase of cell cycle.</td>
<td></td>
</tr>
<tr>
<td>Allicin</td>
<td>Suppress the proliferation of cancer cells and increase apoptosis by activation of caspases.</td>
<td>Oommen, Anto, Srinivas</td>
</tr>
<tr>
<td>S-allyl cysteine</td>
<td>Blockage of nitrosamine generation and bioactivation</td>
<td>Dion et al. (1997)</td>
</tr>
<tr>
<td>Diallyl di sulphide</td>
<td>Colon cancer: suppress the growth of neoplastic CMT-13 cells and N acetyl transferase activity</td>
<td>Chen, Chung, Hsieh</td>
</tr>
<tr>
<td>Diallyl trisulfide</td>
<td>Prostate cancer: increase apoptosis by induction of protein bax and bak</td>
<td>Xiao et al. (S.G. Santhosha)</td>
</tr>
</tbody>
</table>

(10) Prevention against Alzheimer disease

Alzheimer is a form of dementia and amyloid beta(Aβ) deposition (Masters et al., 1985) (Veer Bala Gupta). Alzheimer disease is directly related to psychiatric disease and multifactorial disease. Where almost many allopathic drugs failed to treat Alzheimer but nutraceuticals compounds, phytopharmaceuticals and ayurvedic medicines gave appropriate solution. AGE (aged garlic extract) and SAC (S-allyl cysteine) having anti amyloid property. These two compounds prevent hyperphosphorylation of tau, where tau is a protein helps the brain cells to work prop2.17. erly (Camila Calfio).

Garlic extract (GE) shows variety of properties and prevents cognitive decline by protecting neurons from Aβ neurotoxicity and apoptosis (Borek,2006) Different studies were done to show the positive effect of aqueous garlic extract and boiled garlic extract against the Aβ aggregation. GE and garlic constituents decrease Aβ neuronal apoptosis, by increasing the endogenous antioxidant defences (Peng et al., 2002) (Veer Bala Gupta).

Frequent research proposed that beginning of Aβ amyloid obtain from amyloidogenic processing of β amyloid precursor protein (APP) is the first episode in Alzheimer pathophysiology (Selkoe, 2000).

AGE is having multi phytochemicals like ajoene, polyphenols and also thioureas that possess multiple effects like anti apoptotic etc (Neelima B. Chauhan).

Age garlic extract shows neuroprotective effect as natural NSAID, natural anti apoptotic agent and to enhance memory having combination of single drug or ingredient now used for treatment of Alzheimer (Bordia A. 1978) (S M Shende).

Insulin secretagogue action of garlic compound increase the brain levels of insulin and insulin like growth factor (IGF) which reduce brain Aβ burden and inhibit the activation of GSKβ-3 and can potential Prevent tau phosphorylation(Ray B, Chauhan NB, Lahiri DK).

(11) Role of garlic in wound healing

Wound healing includes exchange between inflammatory cells and extracellular matrix throughout the three phases. These phases are inflammatory phase, proliferative phase and remodelling phase.

A.) During this phase damaged cells and pathogens are eliminate from the site of action.
B.) In proliferative phase, it includes the period of tissue growth that is started in reaction to stimulatory aspect startle assemble throughout the inflammatory phase.Angiogenesis is intermediate to wound healing and includes the generation of capillary blood vessels.

And lastly in remodelling period it includes the regeneration of extracellular matrix, formation of tissues etc.
Early wound healing dependent on angiogenesis and their presence is similar with granulation, migrating fibroblast and new collagen. Impaired angiogenesis is a characteristic of chronic wound encountered with diabetes or artificial insufficiency (Li and Li, 2008; Folkman, 2003, 2007; Rees et al., 1999; Bernstein et al., 1994; Clark et al., 2004; Yamaguchi and Yoshikawa, 2001; Tonnesen et al., 2000; Kubo et al., 2005) (Sohail Ejaz).

Wound healing is a physiological process and the inflammatory cells which increase the rate of healing are cytokines with the help of different pathway like decrease dehydration, increasing granulation tissue formation. Neutrophils release elastase and collagenase and tumour necrosis factor and macrophages appear at the wound site and differentiate into macrophages and secrete cytokines such as TGF-β and VEGF.

Macrophage involved in the phagocytosis and release PDGF, TGF-β, TNF-α, IL-1 AND IL-6 and they helps in the proliferative phase of wound healing. Lymphocytes are essential in the IL-2 formation which helps in recruit fibroblast.

Conventional aqueous antiseptics are not sustainable because the borders of chronic wounds are composed of sclerotic tissue impeding on effectual penetration of the products (Araújo LU; Dorai AA; Shah JM, Omar E; Lee YS, Wysocki A; Bugarza Tepole A; Lademann O, Kramer A) Nader Pazyar

Burns are usually most noxious form of wound and minor burns are usually serve with topical ointments. Higher rate of mortality are because of burn wound difficulties especially to microbial infection. Many of the times wound healing drugs are not partially effective against microorganisms and are also not economically not available for all populations. Garlic has been used from thousands of centuries to treat infectious diseases and having various activities. Allium sativum is the major constituent which posses their activity against microorganisms and to heal wounds.

(Gould LJ., Fulton AT.; Church D, Elsayed S; Somboonwong J; Khashan AA. (Leila Ait Abderrahim)

Garlic possess antioxidant, antiplatelet, antifibrinolytic effect and having impact on microcirculation. Allium sativum consist large amount of allitin, allyl cysteine, allicin etc and these constituents are powerful antioxidants. In further studies it was observed that elevated antioxidants in wounds increase the healing of wounds. Apart from this, anti-inflammatory agents are also play major role in increasing healing of wound. Inflammatory cells like neutrophils, macrophages, lymphocytes etc they play important role to remove the infection by microorganisms and clear cellular debris (Sundaesaran, Subramanian 2003) (Chung, 2006) (Rasik, Shukla, 2000; Farahpour et al., 1015) (Guo, Dipietro) Mohammad Reza Farahpour

In an infected wound, pathogens easily exist in the protective Form which termed as biofilm. Biofilm is fixed in glycocalyx which is a mixture of bacterial secreted extracellular polysaccharide that make a safeguarding matrix adhering to the host surrounding tissue. Acc. To James et al. (2008) generation of polymicrobial biofilm in the chronic wounds such as foot ulcers, pressure ulcers etc.

In the previous studies the activity of Allium sativum and garlic extract (allicin) is to suppressing the generation of bacterial pathogens and allicin also been shown to elevate the susceptibility of P. aeruginosa to tobramycin and to phagocytosis. Garlic extract suppress the P. aeruginosa and Acinetobacter baumannii quorum sensing system they have been there to manage the biofilm enlargement.

In the present studies the activity of garlic ointment is suppressing biofilm growth by gram negative and gram-positive bacteria in in-vitro wound biofilm model. Garlic ointment decrease the biofilm growth and development by S. aureus, Staphylococcus epidermidis, P. aeruginosa etc (Bjarnsholt et al., 2008; Janes et al., 2008) (Stoodley et al., 2002; Sutherland, 2001) (Janes et al) (Al-Waili et al., 2007) (Bjarnsholt et al., 2005; Rasmussen et al.,) (Pushpalatha Nidadavolu).

Some herbs used in the treatment of cutaneous wounds

1.) Lemon  Lee YH, Chang J (140)
2.) Mimosa  Zippel J, Deters A (141)
3.) Soybean  Xu L, Choi TH, (142)
4.) Grape vine  Khanna S, Venojarvi M (143)
5.) Papaya  Nayak BS, Ramdeen R (144)
6.) Ginseng  Kimura Y, Suniyoshi M (145)
7.) Olive oil  Kim HS, Noh SU (146)

(Nader Pazyar)

Conclusion

Wounds are biological process and in the end it causes scar formation. Various medicinal plants verified for healing wounds. Other than healing wounds, in severe conditions medicinal plants are highly effective. Garlic (Allium sativum) Family Liliaceae, a spice widely used all over the world having characteristic odor, produce highly effective action against cancer, act as anti-microbial, anti-fungal, Immune modulator, to prevent cardiovascular disorders. Garlic was also used for workers to increase their work capacity. In the present time, Garlic is still used worldwide as medicinal plant for treating variety of diseases and produce pharmacological effects. As summarized in this review, various properties of garlic. It is clear form the article that garlic in the diet should be considered to be important and mandatory to maintain good health.

Therefore, in the future more biological functions of garlic should be evaluated and more investigations should be conducted to deeply understand the mechanism of action of garlic.

References


Thomas Hess, Cathy BSN, RN, CWOCN Checklist for Factors Affecting Wound Healing, Advances in Skin & Wound Care: April 2011 - Volume 24 - Issue 4 - p 192.


