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### 1. Aloe

Not only a useful cosmetic ingredient: its latex can reduce swelling and diminish pain.



### 2. Achiote

It contains bixin, an anti-inflammatory compound that speeds up collagen maturation, essential for healing.



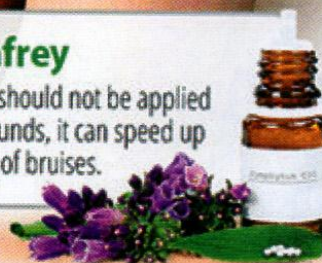
### 3. Garlic

A powerful antiseptic and antibiotic, has been used to disinfect wounds since Ancient Rome.



### 4. Comfrey

Although it should not be applied to open wounds, it can speed up the healing of bruises.



### 5. Calendula

Its petals are antioxidant, anti-inflammatory, and promote skin regrowth.



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# Antioxidants and Wound healing

**SANJAY AGRAWAL**

## Introduction

Wound may be defined as interruptions of cellular and anatomic continuity of living tissue. Wound may arise due to physical, chemical or microbial agents and electrical. Every wound is unique and each deserves individual care. Thus the process of wound healing has been one of the earliest medical problems. It is not wound closure that is important, but it is the quality of the scar and restoration of functional competence that is important. Healing is thus essentially a survival mechanism, and represents an attempt to maintain normal anatomical structure and function. Several scientific studies revealed that many of the plant products are useful in the early and proper maturation of granulation tissue and also enhance the deposition of collagen.

## Background on Indian Medicinal Plants

Medicinal plants are an important element of indigenous medicinal systems in most of the countries including India. India is perhaps the world's largest producer of medicinal herbs and is rightly called the "Botanical Garden of the World". The revival of interest in natural drugs especially those derived from plants started in the last decade mainly because of the widespread belief that "Green Medicines" are healthier and safer than the synthetic ones. In recent

years, the use of such information in medicinal plants research has received renewed interest in the media and in some segments of the scientific community. In the last decade of the 20th century, the "Western" use of such information has come under increasing scrutiny and the national and indigenous rights on these resources have become acknowledged by most academic and industrial researchers. Development of new herbal drugs is a field of intense activity in recent years and hence the need for such basic scientific investigations on medicinal plants used in indigenous medicinal systems becomes ever more evident<sup>1</sup>.

## Oxygen Free Radicals and Wound Healing

Our present day understanding of wound healing has been greatly enhanced over the past 25 years by research elucidating the role of oxygen in this process. Oxygen gradients have been identified across the healing wound, confirming the well perfused periphery of the wound as compared to its relatively anoxic central part<sup>2,3</sup>. Studies modulating the oxygen tension of the wound demonstrate the beneficial effect of increasing the amount of oxygen delivered to the wound and the adverse effect of hypoxia<sup>4</sup>. Despite the beneficial effects of oxygen on collagen synthesis and rates of epithelization, it is also somewhat paradoxically apparent that hypoxic tissue gradients and anaerobic metabolism are important in the initiation of collagen synthesis and angiogenesis. The role of oxygen in preventing wound infection has

similarly been established. All oxygen-dependent mechanisms for intracellular killing by leukocytes result in the generation of highly reactive oxygen metabolites. These oxygen metabolites, collectively termed oxygen radicals, have also been implicated in a variety of ischemic and inflammatory diseases. It is only recently that the effects of these radicals on wound healing have been investigated and clarified. Despite the importance of oxygen in promoting wound healing and preventing wound infection, it is now apparent that oxygen metabolites may in many situations be deleterious to wound healing. Or may result in tissue injury.

Increasing evidence implicates excessive reactive oxygen species (ROS) generation and ROS derived degradation products in the pathogenesis of many skin diseases. Several attempts have been made to identify prognostic biomarkers of wound healing in skin but they are of limited success. Oxygen radicals are produced by the univalent reduction of molecular oxygen, which is catalyzed principally by two enzyme systems, xanthine oxidase and NADPH dehydrogenase. Xanthine oxidase is principally generated in ischemic tissues, whereas NADPH dehydrogenase is a normal component of the neutrophil intracellular killing mechanism. Oxygen radicals are generated principally in ischemic or inflamed tissues. Cells have the ability to protect themselves from these radicals by a variety of enzyme systems. Nevertheless, the production of these highly reactive oxygen metabolites

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can initiate chain reactions that produce further oxidants capable of cellular injury. Oxygen radicals cause tissue injury by lipid peroxidation of membranes at both the cellular and the organelle level by degrading intracellular matrix and by oxidation of important protein and enzyme systems.

#### **Cell Proliferation and Reactive Oxygen Species**

Proliferation of vascular cells is a key feature in vascular biology, wound healing and pathophysiological processes such as atherosclerosis. In atherosclerotic intima, cell proliferation co-localizes with oxidized LDL that indicate a local oxidative stress. During wound healing of confluent cell layer, cell proliferation associated with healing also induced enhanced extracellular ROS generation and LDL oxidation. Proliferation associated extracellular ROS generation is mediated through mitogenic signalling pathways. Data obtained with inhibitors of oxidases suggest that proliferation associated extracellular ROS are not generated by a single ROS generating system and are not essential for cell proliferation. In conclusion, proliferating vascular cells generate high levels of extracellular ROS generating systems by mitogenic signalling. This constitutes a link between proliferative events and oxidative stress, LDL oxidation in atherosclerotic lesions. Antioxidant vitamins, plant products such as carotenoids and polyphenolic flavonoids are potent antioxidant and wound healing substances in nature. As free radical scavengers, flavonoids inhibit lipid peroxidation; promote vascular relaxation to prevent prolonged wound healing. A sufficient supply of antioxidant in diet might help to prevent or delay

the occurrence of pathological changes associated with oxidative stress.

#### **Discussion**

In recent years oxidative stress has been implicated in a variety of degenerative processes, diseases, and syndromes. These include acute and chronic inflammatory conditions including healing of wounds<sup>5, 6</sup>. The oxidants rich at the wound site were contributed mostly by macrophages and neutrophils<sup>7</sup>. Molecular oxygen plays a central role in the pathogenesis and therapy of chronic wounds. Overproduction of reactive oxygen species (ROS) results in oxidative stress thereby causing cytotoxicity and delayed wound healing.

Therefore, elimination of ROS could be an important strategy in healing of chronic wounds<sup>8</sup>. Oxygen free radicals play an important role in the failure of ischemic wound healing. Studies have shown that antioxidants improve the healing in ischemic skin wounds<sup>9</sup>. Low levels of antioxidants accompanied by raised levels of markers of free radical damage play a significant role in delaying wound healing in rats<sup>10</sup>. Therefore estimation of antioxidants like SOD, catalase and glutathione peroxidase in granulation tissues is also relevant because these antioxidants hasten the process of wound healing by destroying the free radicals. Increasing evidence implicates excessive ROS generation and ROS derived degradation products in the pathogenesis of many skin diseases. The significant alteration in the antioxidant profile accompanied by the elevated levels of MDA, a marker of free radical damage, may be attributed to impaired wound healing in immunocompromised rats. Numerous attempts have

been made to identify prognostic biomarkers of wound healing in skin; these have met with limited success. A recently coined term "Nutraceuticals" describes a variety of nonprescription products, which include mainly flavonoids to enhance health. Antioxidant properties of natural products and medicinal herbs were evaluated mainly by assessing the direct scavenging action of in vitro generated free radicals and inhibition of lipid peroxidation and assessing indirectly the effect of that compound on endogenous antioxidant defenses. Several antioxidants are ingredients of our daily diet and/or cellular components eg. Carotenes, vitamins A, C, E and flavonoids. The flavonoids are a heterogenous group of ubiquitous plant polyphenols that abound in the human diet and are endowed with the several biological activities including immunomodulating and antioxidant activities. Study of 12 different plant flavonoids has revealed that there in vitro antioxidant activity also works under in vivo conditions. Flavonoids have been reported to protect against oxidative stress. A detailed review indicates the presence of flavonoids, which is responsible for the antioxidant and wound healing activities. Flavonoids are the plant pigments, which have the ability to inhibit specific enzymes and to scavenge free radicals which may ultimately help in the healing of wounds<sup>11, 12</sup>.

As free radical scavengers, Flavonoids inhibit lipid peroxidation, promote vascular relaxation and help to prevent prolonged wound healing. A sufficient supply of antioxidant in the diet might help to prevent or delay the occurrence of pathological changes associated with oxidative stress. Natural

antioxidants from plants strengthen the endogenous antioxidant defenses from ROS ravage and restore the optimal balance by neutralizing the reactive species. They are gaining immense importance by virtue of their critical role in disease prevention. In my study of wound healing and indigenous drugs, I have evaluated the wound healing efficacy and antioxidant properties of 10 different plants namely *Aristolochia bractolata* (Aristolochiaceae), *Calotropis procera* (Asclepiadaceae), *Centella asiatica* (Umbelliferae), *Glycyrrhiza glabra* (Leguminaceae), *Hyptis suaveolens* (Labiaceae), *Jatropha curcas* (Euphorbiceae), *Ocimum sanctum* (Labiaceae), *Phyllanthus niruri* (Euphorbiceae), *Tinospora cordifolia* (Menispermaceae) *Withania somnifera* (Solanaceae). Among the 10 indigenous plants

used for screening studies, the crude extract of *Ocimum sanctum* exhibited significant prohealing activities, which was superior to remaining plant extracts investigated.

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## ANNOUNCEMENT

We are happy to announce to our Readers that we are going to re-introduce soon the page “**Correspondence**” in our journal “The Antiseptic”, in which we will publish the questions of readers with answers to the same by the specialists of respective field of medicine and surgery.

Readers are intimated that they may send their questions to the following address.

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