

**Review Article****Some promising medicinal plants with anti-diabetic wound healing activity: A review**

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**Abstract**

Diabetes mellitus (DM) is chronic disease of endocrine system and one of life threatening problems of the modern era, characterised by high level of glucose in blood. Diabetic patients have the enormous risk of serious infective foot ulcer or wound. The poor wound healing and ineffective functioning with infection in diabetic patient can cause gangrene and finally lead to limb amputation. Herbal medicine, also known as phytomedicine, have been widely used since the ancient times. Studies has been proved that the medicinal plants are rich sources of chemical substances with potential therapeutically and pharmacological activity for treatment of many diseases. Plant shows the presence of various life-sustaining constituents which have potential diabetic wound healing properties. Herbal preparation can be more effective than conventional medicines These phytomedicines are not only cheap and affordable but are also safe. Considering these facts the present review aims to reveal the up to date literature on recent ethnomedical uses with phytochemical review of two different medicinal plants *Catharanthus roseus*, *Terminalia chebula* which are commonly used for treatment diabetic wound healing in ayurvedic system of medicine.

**Keywords:** Diabetes mellitus (DM), *Catharanthus roseus*, *Terminalia chebula*

**Introduction**

Diabetes mellitus is a chronic endocrine disorder, characterized by hyperglycaemia resulting from absolute or relative insulin deficiency. Uncontrolled diabetes can lead to a number of short and long-term health complications, including hypoglycemia, heart disease, nerve damage and amputation, and vision problems. Major increase in mortality of Diabetes is due to the development of both macro and micro vascular complication including failure of wound healing. Experts suggest that around 10 per cents of people with diabetes develop a foot ulcer at some point.

Foot ulcers can affect people with both type 1 and type 2 diabetes (Okonkwo and DiPietro, 2017). People with diabetes may have reduced nerve functioning due to peripheral diabetic neuropathy.

This means that the nerves that usually carries pain sensation to the brain from the feet do not function as well and it is possible

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for damage to occur our foot without feeling it (David and Greenhalgh, 2003). Treading on something, wearing tight shoes, cuts, blisters and bruises can all develop into diabetes foot ulcers. Narrowed arteries can also reduce blood flow to the feet amongst some people with diabetes and this can impair the foot's ability to heal properly (Gowthamarajan et al., 2015). When the foot cannot heal, a foot ulcer can develop.

The aim of this review is to provide information on the Phytochemicals, Ethnomedicinal uses and Pharmacological activities of two medicinal plants (*Catharanthus roseus*, *Terminalia chebula*) commonly used in Aurvedic medicine for the treatment of diabetes mellitus wound healing (Sharma et al., 2013).

***Terminalia chebula***

*Terminalia chebula* is a flowering deciduous tree of the family combrataceae. According to hindu mythology the plant is considered as it is originated from the drops of amrita so it is called king of medicines. The Terminalia consists of 250 species and widely distributed in tropical areas of the world (Rathinamoorthy and Thilagavathi, 2014).

**Macroscopic character** (Dodke and Pansare, 2017; Baliah and Astalakshmi, 2014)

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**Figure 1.** (a) *Terminalia chebula* fresh fruits (b) *Terminalia chebula* dried fruits

**Tree:** medium to large sized highly branched deciduous tree with dark brown coloured stem having longitudinally cracked woody scales. Stem is dark brown usually longitudinally cracked.

**Leaves:** Leaves is 10-30 cm long having alternative to sub opposite arrangement with broad petiole. 6 to 8 pairs of veins are seen in each leaf let with an acute tip and cordate base.

**Flower:** flowers is dull white to yellowish colour and monocious in nature having strong unpleasant odour.

**Fruits:** The fruit is smooth ellipsoid to ovoid drupes, yellow to orange brown in colour and having blackish, with five longitudinal ridges. Color yellowish, odour was characteristic and taste was found bitter.

**Table 1.** Taxonomic Classification (Singh and Malhotra, 2017)

Kingdom	Plante
Sub kingdom	Viridiplante
Infrakingdom	Streptophyta
Super division	Embryophyta
Division	Tracheophyta
Sub division	Spermatophyte
Class	Magnoliopsida
Super oder	Rosanae
Order	Myrtales
Family	Combrataceae
Genus	<i>Terminalia</i>
Species	<i>Terminalia chebula</i>

### Ethanomedical review

*Terminalia chebula* is one of the most commonly used plants in traditional systems of medicine in Indian sub continent and is also called “King of the medicine (Surya Prakash, et al., 2012) due to its wide range of phytochemical and pharmacological properties. The plant haritaki is an all rounder its one of the listed medicine in ayurvedic Meteria medica for the treatment of vomiting, gout, asthma, bleeding piles etc. it act as a natural laxative because it contain large amount of fibers. It also a well known blood purifier. As per thai medicine it act as carminative expectorant. Fruit extract posses anti cancer activity,

antioxidant, cytoprotective activity, antispasmodic, cardiotoxic activity and wound healing activity (Soni et al., 2013).

Fruits of *Terminalia* is used internally and externally of different purpose it is a great wound healer in diabetic as well as normal wound it fastness the re epithelisation (Muhammad et al., 2012) and promote wound healing, and it have broad spectrum of anti bacterial activity. It is good for vision power, anti- aging, rejuvenative, and it improves life expectancy, nourishing, and the body weight.

**Table 2.** Vernacular names of *Terminalia chebula* (Kumar and Kumar, 2017)

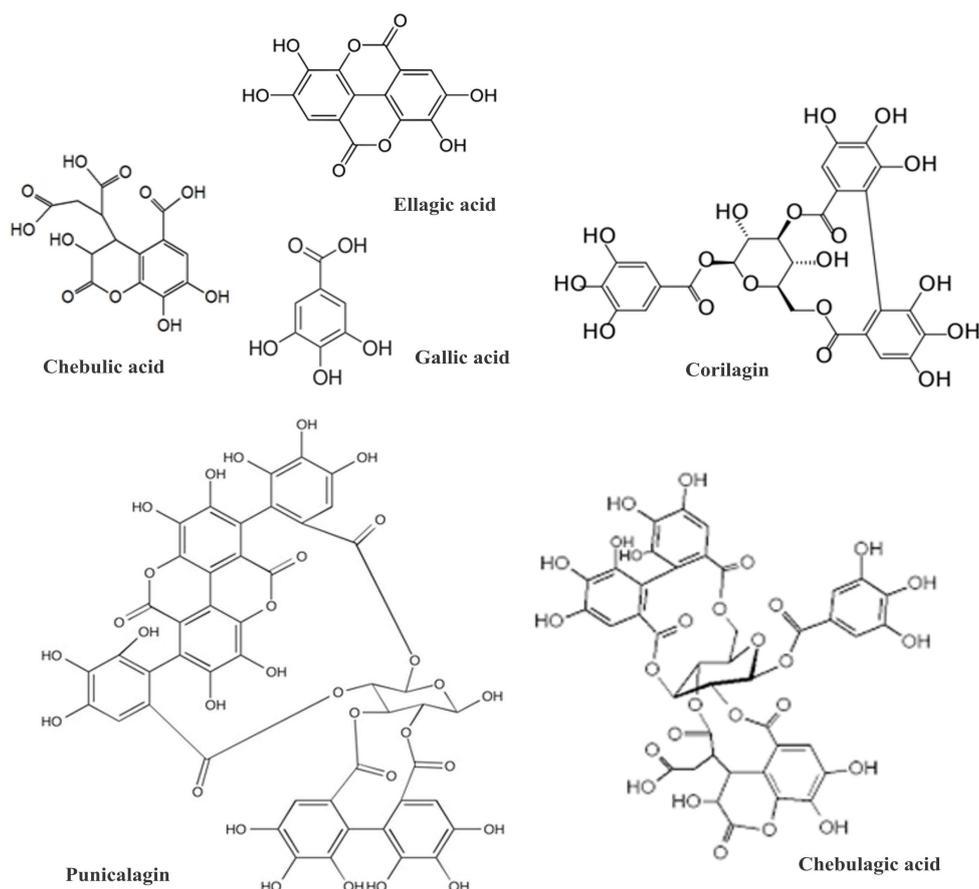
Language	Name
Malayalam	Katukka
Hindi	Harra, harad
Sanskrit	Kayastha, jivapriya
Bengali	Haritaki
Kannada	Halle
Tamil	Kadukkay
Telugu	Nallakaraka
Marati	Hirad
Manipuri	Manahi
Oriya	Karedha

### Phytochemical review

*Terminalia chebula* contain several phytochemicals such as tannins fructose amino acids, resins flavonoids, sterols, but the major constituent is tannin approximately 32 percentage, the tannin contents varies according to the geographical locations. Phytochemicals like amino acids fructose resins fixed oil, carbohydrates etc are also present in this plant, *Terminalia chebula* is a rich source of hydrolysable tannin like gallic acid, chebulic acid, punicalagin (Figure 2), chebulanin, corilagin, neochebulinic, ellagic acid, chebulagic acid, 1,2,3,4,6 - penta-O-galloyl-β-D-glucose 1,6-di-O-galloyl-D-glucose and Terchebulin. These are responsible for pharmacological activities. Phytochemicals like anthraquinone ethadiolic acid, sennoside, 4,2,4-chebylyl-d-glycopyranose terpenes and terpinols have also been reported. Some other minor chemical constituents were polyphenols such as corilagin, gallolyl glucose, punicalagin, terflavin A, maslimic acid. Fructose, amino acid, succinic acid, betasitosterol.

### Anti-diabetic wound healing activity

*Terminalia chebula* were a potent source of antioxidative phenolic compounds that counteract with reactive oxygen species responsible for delayed wound healing. The fruits



**Figure 2.** Major chemical constituents of *Terminalia chebula*

of *Terminalia chebula* significantly increased the level of superoxide dismutase, nitric oxide and decreased lipid peroxidation in granuloma tissue of diabetic mice. It promotes wound healing by reduction in blood glucose level, rapid contraction of wound area and increased granulation of tissue with elevated tensile strength.

Singh (2017) conducted a study on *Terminalia chebula* and summarise that the plant have a role in diabetic wound healing. Diabetic is induced on rat using streptozotocin. For the preparation of methanolic plant extract, soxhlet method was employed. Then the extract is subjected to phytochemical analysis. The extract shows the presence of alkaloid tannin, steroid, saponins, flavanolid. A wound having 1 cm thickness was made in the mid-dorsum region of each rat and wound diameter is taken in 3d 7<sup>th</sup> and 13<sup>th</sup> day. Intraperitoneal administration of methanolic extract of *Terminalia chebula* shows decrease in blood glucose level. When the dose was increases the hypoglycemic effect also increases. Study reveals that the hypoglycemic effect is due to the presence of secondary metabolites present in the plant such as flavonoid, terpenoid, tannins, phenolic compounds alkaloid etc. It helps in the regeneration of beta cells in the islets of Langerhans. Intreperitoneal injection of extract accelerate the wound contraction in diabetic mice. The wound healing power is due to

the presence of alkaloid tannins phenols which increases the epithelisation and collagen synthesis responsible for wound healing. Study says the herbal extract increase the amount of SOD and NO which stimulate the oxygen supply to the wound and accelerate the wound healing.

Singh (2009) conducted a study to determine the of wound healing potency of *Terminalia chebula* in diabetic rat. Alloxan is the chemical used to induce diabetic in rat. For this ethenolic extract were prepared using cold maceration process the , powdered drug is soaked in 250 ml of hydroalcoholic solution(50%) for 2 day and the crude extract is used for the study. The excision and dead space wound models are employed to evaluate the diabetic wound healing potency of *Terminalia chebula*. For this study Sprague Dawely verity of rats are used. The wound healing property of *Terminalia chebula* seed extract with liquid paraffin ointment base is applied on the excision wound and the wound contraction is noted .mupirocin ointment was used as a standard. The study reveals that there is significant increase in the wound contraction in rat treated with extracts. The study says that the effective wound contraction is mainly due to presence of phytoconstituents such as phenols tannin and terpenoid. The study concluded that in excision and dead space wound model the wound

closure is higher when compared to control group.

### *Catharanthus roseus*

*Catharanthus roseus* is an evergreens shrub of the family apocynaceae. There are 8 species (Das and Sharangi, 2017) of catharanthus, 7 species are endemic to Madagascar and one is endemic to india (*C. pusillus*). *Catheranthus roseus* have long history. The plant was traced by Mesopotominanns at 2600 bc. Based on the colour there are 2 main species *Cartharanthus roseus* having pink and *Catharathus alba* having white colour. *C Roseus* is the rich source of alkaloid so that the plant plays key role in world health care.



**Figure 3.** Flowers of *Catharanthus roseus*

### Macroscopic character (Goswami, 2016)

**Plant:** It is evergreen shrub having 1 m hight.

**Leaves:** Leaves is oval to oblongs, glossy green hairless, 2.5-9 cm long having opposite arrangement. Leaves powder showed green in color, odour was characteristic and taste was found bitter (Gilman and Howe, 1999).

**Flowers** (Tolambiya and Mathur, 2016): flowers are pink in colour with dark red at the center consist of 5 petals and having strong unpleasent odour.

**Table 3.** Taxonomical Classification (Gilman and Howe, 1999)

Kingdom	Plantae
Subkingdom:	Tracheobionta
Super division:	Spermatophyta
Division:	Magnoliophyta
Class:	Magnoliopsida: dicotyledons
Subclass:	Asteridae.
Superorder:	Gentiananae.
Order:	Gentianales.
Family:	Apocynaceae
Genus:	<i>Catharanthus</i>
Species	<i>Catharanthus roseus</i>

**Table 4.** Vernacular names of *Catharanthus roseus* (Retna and Ethalsha, 2013)

Language	Name
Malayalam	Nithyakalyani, savakottapacha,Ushamalari
Hindi	Sadabahar,Baramassi,Ainskati
Sanskrit	Nithyakalyani
Bengali	Nayanthara
English	Bright-eyes, Cape periwinkle, graveyard plant, Madagascar periwinkle, old-maid,
Tamil	Sudukattu Mallikai
Telugu	Billaganneru
Marati	Sada-phul (Sadaphuli)
Punjabi	Rattan jot
Konkani	Sadapushpa

### Ethanomedical review

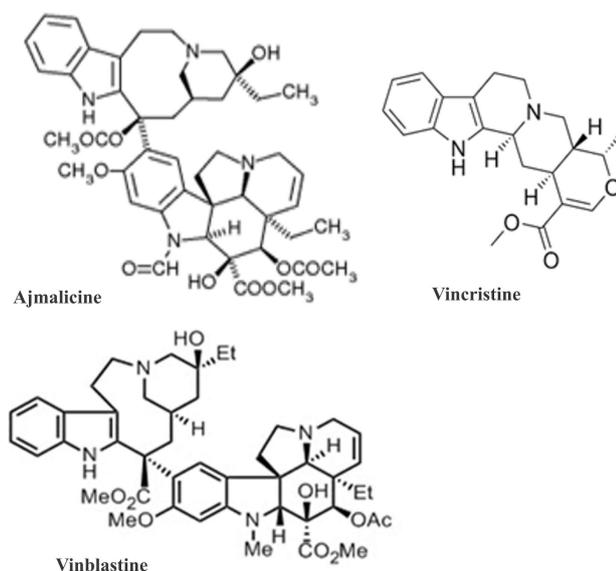
*Catharanthus roseus* is well known plant for cancer treatment. The alkaloid, vincristine and vinblastine obtained from this plant acts by arresting mitosis the metaphase (Kokate et al.,). It is given intravenously in the treatment of acute leukaemia of children. The plant extracts posses anti diabetic, anti helminthic, anti oxidant anti diarrhoeal properties. The roots of the plant was found to accumulate ajmalicine and serpentine, which are the important components of medicines that are used for controlling high blood pressure and other types of the cardio-vascular problems and it used in the treatment of gastritis, cystitis, enteritis, memory loss, toothache, circulatory disorders, chest complaints, throat infections, Treats nose bleed, bleeding gums and haemorrhoids, eye infection and eye irritation (Nayak, 2006) and Relieves symptoms of skin diseases such as acne, dermatitis and eczema also Quickens healing process and stops bleeding (Sain and Sharma, 2013; Singh et al., 2014).

### Phytochemical review

A large number of indole alkaloids is present in vinca. Out of them about 20 dimeric (Sain and Sharma, 2013) indole dihydroindole alkaloid posesesses oncolytic activity, and among them, vincristine and vinblastine are most significant. Vinblastin contains indole alkaloid part called catharanthine and dihydroindole alkaloid part vindoline. The other alkaloid present in vinca is ajmaline, lochnerine, serpentine (Balaji, 2014), and tetrahydroalstonine. It requires about 500mg crude drug to extract out 1 g of vincristine, Because of its extreame low content ie. 0002 per cent. This makes these alkaloids very costlier.

### Anti-diabetic wound healing activity

The wound-healing property of *C. roseus* may be attributed to the phytoconstituents present in the plant, and the quicker



**Figure 4.** Major chemical constituents of *Catharanthus roseus*

process of wound healing could be a function of either the individual or the additive effects of the phytoconstituents. Recent studies have shown that phytochemical constituents like flavonoids and tri-terpenoids are known to promote the wound-healing process mainly due to their astringent and antimicrobial properties which appear to be responsible for wound contraction and increased rate of epithelialisation.

Singh et al. (2014) examined the methanolic extract of leaves of *Catharanthus roseus* for antidiabetic wound healing activity. The diabetic wound healing property of *Catharanthus roseus* leaf are studied using excision wound model. The wound was inflicted by cutting 1 cm diameter of the skin on the mid- dorsum region of the rat and the wound contraction is observed during 1st, 7<sup>th</sup> and 13<sup>th</sup> day. In this study investigated that *Catharanthus roseus* accelerate wound healing and also reduces the blood sugar level. The study revealed that the methanolic extract of 1 fresh leaves increases the tensile strength, hydroxyproline content in rats. The primary phytochemical screening of leaves shows the presence of tannin alkaloid and terpenoid the result revealed that these are the compound responsible for anti diabetic wound healing activity.

Nayak et al. (2006) studied antimicrobial and wound healing activity of flower extract of *Catharanthus roseus* in Sprague Dawley rats. Three wound models such as Excision, incision and dead space were used to assess the wound-healing activity of *Catharanthus roseus* flower extract. In excision wound model a wound having circular area of 300mm was made on the back of the animal, in the case of incision wound model. A longitudinal paravertebral incision, six centimetres in length was made through the skin and cutaneous muscle and all groups are treated with increasing concentration of extract. This study revealed that the plant have the potential to accelerate the wound healing and it

increase the tensile strength and hydroxyproline content in sparague dawly rats.

A study was conducted to determine Influence of Ethanol Extract of *Vinca rosea* on Wound Healing in Diabetic Rats. The diabetic wound healing property of *Catharanthus roseus* leaf extract (topical application) was studied using streptozotocin induced excision wound. Vasline was the control formulation. The rat was induced by diabetic using intraperitoneal single dose injection of streptozotocin. Wound was created on the back having full thickness of 2.5 cm and depth of 0.2 cm. Leaves extract was applied for 10 days and wound contraction was measured during first fifth and leventh day using transparent marker. The phytochemical study of *Catharanthus roseus* reveals that the extract has the presence of alkaloid tannin and triterpenoid. The study concluded that these are the compound responsible for diabetic wound healing. The study investigated that the plant has the capacity to increase the epithelisation and increase the blood flow and oxygen supply to the wound by blocking the vasoconstructive compounds.

### Conclusion

Diabetes is the leading cause of nontraumatic lower extremity amputations in the world wide, with approximately 5% of diabetics developing foot ulcers each year and 1% requiring amputation. In this review article, an in depth study on ethnobotanical uses, phytochemical constituents and pharmacological activities of two major diabetic wound healing plants namely, *Catheranthus roseas*, *Terminalia chebula* have been done.

Nowadays, the demand for natural products and plant based medicines is growing throughout the world. Herbal

preparation can be more effective than conventional medicines and their non-toxic nature means that they can be administered over long period.

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**Conflicts of interest:** Nil

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