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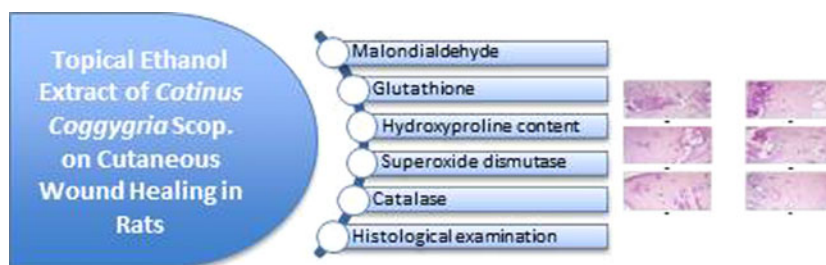
SHORT COMMUNICATION

The effect of topical ethanol extract of *Cotinus coggygia* Scop. on cutaneous wound healing in rats

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The aim of this study is to determine the cutaneous wound healing effects of the ethanol extract of *Cotinus coggygia* leaves in rats by excision wound model to provide scientific evidence for the traditional use of *C. coggygia* Scop. The levels of malondialdehyde, catalase, superoxide dismutase, glutathione and hydroxyproline were investigated in wound tissues. Histopathological examination was also performed. The hydroxyproline content of the granulation tissue and the glutathione levels were both significantly higher in the treatment group than in the control group ($p < 0.05$ for both); while the malondialdehyde levels were significantly lower in the treatment group ($p < 0.05$). These results were supported with histological results. The ethanol extract of *C. coggygia* Scop could be considered as an effective agent in wound healing in accordance with its traditional use.

Keywords: wound healing; hydroxyproline; *Cotinus coggygia* Scop

1. Introduction

The leaves of *Cotinus coggygia* have been used in traditional folk medicine as antipyretic, antiseptic, anti-haemorrhagic and in treatment of diarrhoea and wound healing (Baytop 1999; Kültür & Bitiş 2007). According to previous studies about phytochemical investigation of *C. coggygia*, it is seen that gallic tannins, flavonoids, anthocyanins and terpenes in essential oil are chemical constituents of *C. coggygia* (Westernburg et al. 2000; Demirci et al. 2003; Kültür & Bitiş 2007). It was found that *C. coggygia* extract has high total antioxidant activity and free

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radical scavenging activity, which is attributed to its high amount of total phenols and flavonoid content (Nićiforović et al. 2010). To our knowledge, the cutaneous wound healing effects of the ethanol extract of *C. coggygia* Scop. have not been studied *in vivo* before. Therefore, in this study the effect of ethanol extract of leaves of *C. coggygia* on excision wound model has been investigated to provide scientific evidence for its traditional use.

2. Results and discussion

Wound healing process involves inflammation, granulation, collagenisation, collagen maturation and scar maturation, respectively. Various herbal ointments used in the folk medicine have been reported to be effective in wound healing (Ghosh et al. 2012). The normal wound healing process could be based on collagen's production, deposition and also subsequent maturation. Hydroxyproline is an essential component of collagen structure, and is attributed to approximately 14% (Upadhyay et al. 2013). Increases in collagen and hydroxyproline concentration during granulation tissue formation have been reported with topical administration of some herbal extracts in previous studies (Sadaf et al. 2006; Pattanayak & Sunita 2008; Srinivas et al. 2008). In this study, the hydroxyproline content in the granulation tissue of rats was significantly higher in the treatment group than in the control group after the 3rd day and 14th day (2.50 [2.30–3.03] vs. 1.90 [1.50–2.08]; $p < 0.01$ and 6.40 [6.38–7.13] vs. 6.00 [6.00–6.13], $p < 0.05$; respectively) (Table S2). The latest studies have indicated that phytochemical compounds such as flavonoids and terpenoids accelerated wound healing by contracting the wound and elevating the epithelialisation due to their astringent and antimicrobial properties. The compounds found in the plant might have contributed to the wound-healing property of *C. coggygia* and the accelerated wound-healing process might be attributed to either individual or combined effects of the compounds existing in the plant (Jain et al. 2010).

The effect of antioxidant treatment in wound healing has been shown in previous studies with reduction of oxidative stress and enhancement of antioxidant activity (Panchatcharam et al. 2006; Pattanayak & Sunita 2008; Kokane et al. 2009; Chaturvedi et al. 2012; Cetin et al. 2013). It was shown that topical administration of a substance with free-radical-scavenging properties significantly recovered wound healing and defended tissues from oxidative damage in patients (Kumar et al. 2007).

In our studies, a statistically significant elevation in glutathione (12.50 [10.00–13.25] vs. 5.00 [1.75–9.25], $p < 0.05$; 13.50 [12.00–15.00] vs. 4.50 [3.50–5.00], $p < 0.01$; 6.50 [4.00–9.25], $p < 0.05$, respectively) and a statistically significant decrease in malondialdehyde levels (2.50 [2.00–5.00] vs. 9.50 [7.25–11.75], $p < 0.01$; 11.50 [10.00–15.00] vs. 17.25 [14.75–17.88], $p < 0.05$; 11.00 [10.58–12.35] vs. 12.65 [11.88–27.75], $p < 0.05$; respectively) were determined in the *C. coggygia* treatment group when compared with the control group at the end of 3rd, 7th and 14th days ($p < 0.05$) (Table S3). Superoxide dismutase and catalase activity have been detected with high levels of herbal medicines containing phenolic components in wound healing studies (Chaturvedi et al. 2012). Previous studies showed that reactive oxygen species scavenging enzymes such as superoxide dismutase, catalase and glutathione peroxidase have a major role during wound healing process especially at the early stage of wound healing (Steiling et al. 1999). On the other hand, different types of phenolic compound functional groups have a capacity of chelation of metal ions such as Fe(II), Cu(II) and Zn(II) (Nest et al. 2004; Karamać 2009) and these compounds have the ability to scavenge free radicals. It is known that *C. coggygia* contains a variety of effective polyphenols as dominant constituents. Superoxide dismutase and catalase depend on the metal cofactor. Therefore, in this study, superoxide dismutase (3.94 [3.78–4.06] vs. 3.78 [2.84–4.33]) and catalase levels (9.35 [5.74–24.87] vs. 6.58 [5.99–9.65]) increased on the 7th day when compared with the control group; but these

increases were not statistically significant (Table S3). Recent studies have shown that *C. coggygia* has a potential effect on antioxidant enzymes using various different animal models (Li et al. 2011; Matic et al. 2011; Yarat et al. 2013). These results showed that *C. coggygia* acts as a powerful antioxidant, which would be effective in preventing oxidative damage and promoting the healing process.

In rats, neutrophils appeared in the wound lesion 4–6 h after injury and increased in number on the first day (Taoka et al. 1997; Carlson et al. 1998). Inflammation does not persist unless the wound gets chronic (Tregrove et al. 1999). Normally, inflammatory phase ceases before granulation phase starts (Singer & Clark 1999). The granulation phase involves recruitment of fibroblasts, angiogenesis and reepithelialisation. Remodelling and contraction of the granulation tissue result in an organised network of collagen and elastin fibres, leading to the formation of scar tissue (Jackson et al. 2005). However, abundant granulation tissue and excessive fibrosis lead to scar formation and loss of function (Stadelmann et al. 1998).

The phases of the wound healing may overlap each other during normal wound healing, however they need to occur in an order. Any problem occurring during these delicate events will lead to impaired wound healing. Decreased oedema on 3rd day, decreased fibroblast density on 14th day, decreased neutrophil infiltration on 3rd day and increased angiogenesis on both the 7th and 14th days in the experiment group compared with the controls of the same days in our experiment explain the mechanism of treatment promoting wound healing.

3. Conclusion

Ethanol extract of *C. coggygia* could be considered as an effective agent in wound healing. These results also confirm the traditional use of these plants. Further studies will be designed to investigate dose-dependent effect of the ethanol extract of *C. coggygia* in cutaneous wound healing and delayed-wound healing models. The possible effects of *C. coggygia* would be investigated in different wound models (e.g. ulcer, colitis) by using various vehicle systems.

Supplementary material

Experimental methods would be found online, alongside Tables S1–S3 and Figure S1.

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References

- Baytop T. 1999. Therapy with medicinal plants in Turkey past and present. 2nd ed. İstanbul: Tıp Basımevi.
- Carlson SL, Parrish ME, Springer JE, Doty K, Dossett L. 1998. Acute inflammatory response in spinal cord following impact injury. *Exp Neurol*. 151:77–88.
- Cetin EO, Yesil-Celiktas O, Cavusoglu T, Demirel-Sezer E, Akdemir O, Uyanikgil Y. 2013. Incision wound healing activity of pine bark extract containing topical formulations: a study with histopathological and biochemical analyses in albino rats. *Pharmazie*. 68:75–80.
- Chaturvedi AP, Kumar M, Tripathi YB. 2012. Efficacy of *Jasminum grandiflorum* L. leaf extract on dermal wound healing in rats. *Int Wound J*. 10:675–682.
- Demirci B, Demirci F, Başer KHC. 2003. Composition of the essential oil of *Cotinus coggygia* Scop. from Turkey. *Flavour Fragr J*. 18:43–44.
- Ghosh S, Samanta A, Mandal NB, Bannerjee S, Chattopadhyay D. 2012. Evaluation of the wound healing activity of methanol extract of *Pedilanthus tithymaloides* (L.) Poit leaf and its isolated active constituents in topical formulation. *J Ethnopharmacol*. 142:714–722.

- Jackson CJ, Xue M, Thompson P, Davey RA, Whitmont K, Smith S, Buisson-Legendre N, Szynda T, Furphy LJ, Cooper A, Sambrook P, March L. 2005. Activated protein C prevents inflammation yet stimulates angiogenesis to promote cutaneous wound healing. *Wound Repair Regen.* 13:284–294.
- Jain N, Jain R, Jain A, Jain DK, Chandel HS. 2010. Evaluation of wound-healing activity of *Acorus calamus* Linn. *Nat Prod Res.* 24:534–541.
- Karamać M. 2009. Chelation of Cu(II), Zn(II), and Fe(II) by Tannin constituents of selected edible nuts. *Int J Mol Sci.* 10:5485–5497.
- Kokane DD, More RY, Kale MB, Nehete MN, Mehendale PC, Gadgoli CH. 2009. Evaluation of wound healing activity of root of *Mimosa pudica*. *J Ethnopharmacol.* 124:311–315.
- Kültür Ş, Bitiş L. 2007. Anatomical and preliminary chemical studies on the leaves of *Cotinus coggygia* Scop. (Anacardiaceae). *J Faculty Pharm Istanbul.* 39:65–71.
- Kumar B, Vijayakumar M, Govindarajan R, Pushpangadan P. 2007. Ethnopharmacological approaches to wound healing – exploring medicinal plants of India. *J Ethnopharmacol.* 114:103–113.
- Li Y, Zhao H, Duan B, Korpelainen H, Li C. 2011. Effect of drought and ABA on growth, photosynthesis and antioxidant system of *Cotinus coggygia* seedlings under two different light conditions. *Environ Exp Bot.* 71:107–113.
- Matić S, Stanić S, Bogojević D, Vidaković M, Grdović N, Arambašić J, Dinić S, Uskoković A, Poznanović G, Solujić S, et al. 2011. Extract of the plant *Cotinus coggygia* Scop. attenuates pyrogallol-induced hepatic oxidative stress in Wistar rats. *Can J Physiol Pharmacol.* 89:401–411.
- Nest G Le, Caille O, Woudstra M, Roche S, Burlat B, Belle V, Guigliarelli B, Lexa D. 2004. Zn–polyphenol chelation: complexes with quercetin, (+)-catechin, and derivatives: II electrochemical and EPR studies. *Inorg Chim Acta.* 357:2027–2037.
- Ničiforović N, Mihailović V, Masković P, Solujić S, Stojković A, Pavlović Muratspahić D. 2010. Antioxidant activity of selected plant species; potential new sources of natural antioxidants. *Food Chem Toxicol.* 48:3125–3130.
- Panchacharam M, Miriyala S, Gayathri VS, Suguna L. 2006. Curcumin improves wound healing by modulating collagen and decreasing reactive oxygen species. *Mol Cell Biochem.* 290:87–96.
- Pattanayak SP, Sunita P. 2008. Wound healing, anti-microbial and antioxidant potential of *Dendrophthoe falcata* (L.f) Ettingsh. *J Ethnopharmacol.* 120:241–247.
- Sadaf F, Saleem R, Ahmed M, Ahmad SI, Navaid-ul Z. 2006. Healing potential of cream containing extract of *Sphaeranthus indicus* on dermal wounds in Guinea pigs. *J Ethnopharmacol.* 107:161–163.
- Singer AJ, Clark RA. 1999. Cutaneous wound healing. *N Engl J Med.* 341:738–746.
- Srinivas RB, Kiran KRR, Naidu VG, Madhusudhana K, Agwane SB, Ramakrishna S, Diwan PV. 2008. Evaluation of antimicrobial, antioxidant and wound-healing potentials of *Holoptelea integrifolia*. *J Ethnopharmacol.* 115:249–256.
- Stadelmann WK, Digenis AG, Tobin GR. 1998. Physiology and healing dynamics of chronic cutaneous wounds. *Am J Surg.* 176:26S–38S.
- Steiling H, Munz B, Werner S, Brauchle M. 1999. Different types of ROS-scavenging enzymes are expressed during cutaneous wound repair. *Exp Cell Res.* 247:484–494.
- Taoka Y, Okajima K, Uchiba M, Murakami K, Kushimoto S, Johno M, Naruo M, Okabe H, Takatsuki K. 1997. Role of neutrophils in spinal cord injury in the rat. *Neuroscience.* 79:1177–1182.
- Trengove NJ, Stacey MC, MacAuley S, Bennett N, Gibson J, Burslem F, Murphy G, Schultz G. 1999. Analysis of the acute and chronic wound environments: the role of proteases and their inhibitors. *Wound Rep Reg.* 7:442–452.
- Upadhyay A, Chattopadhyay P, Goyary D, Mazumder PM, Veer V. 2013. *Eleutherine indica* L. accelerates *in vivo* cutaneous wound healing by stimulating Smad-mediated collagen production. *J Ethnopharmacol.* 146:490–494.
- Westernburg HE, Lee KJ, Lee SK, Fong HHS, Bremen RBV, Pezutto JM, Kinghorn AD. 2000. Activity-guided isolation of antioxidative constituents of *Cotinus coggygia*. *J Nat Prod.* 63:1696–1698.
- Yarat A, Sacan O, Akyuz S, Alev B, Pisiriciler R, Ak E, Yanardag R. 2013. *In vitro* effect of aqueous plant extracts on antioxidant parameters in saliva samples. *J Med Plants Res.* 7:118–125.