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Design of new cream formulations with natural products and assessing their effectiveness on wound healing by using *in-vivo* animal model

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Abstract

Since ancient times, people have utilized some plants and their preparations in order to treat their wounds. Often their use is only based on tradition, without any scientific evidence of efficacy and little knowledge about default active compounds or their mode of actions. In this study, the balsam (Levant storax), produced by injuring the oriental sweeet gum trees, was formulated in a wound care cream to evaluate its wound healing effects. Another cream (Complex) was also designed to contain calendula oil, *St. John's Wor*t extract, escin, freeze dried powder of *Aloe vera* (L.) Burm.f. leaf juice and allantoin to evaluate its wound healing potential. Following the development of cream formulations of Levant storax, complex and placebo (without active ingredients), the characterization and stability tests were performed at predetermined time and conditions. The wound healing potential of Levant storax and complex creams were tested against a reference cream Madecassol®, negative control and placebo cream by employing an *in-vivo* excision wound model on rats. Six male Sprague–Dawley rats were used for each treatment group by making six wounds on the back of the animals with 5 mm punches (Figure 1). All groups were treated by applying the test products topically once a day till the wounds of one of the groups were completely healed. The progressive changes in wound area were measured by a standard reference ruler and monitored by the means of the photographs taken from the wounds every other day. The wound areas were computed by using the Image J software and the wound contraction rates were calculated as a percentage of the reduction in wounded area and analyzed for statistical significance by using one way ANOVA. At the end of the treatment schedule, all groups were sacrificed by injection of high dose aneshesia and tissue specimens were isolated from the healed skin of each wound for histopathological examination. The histopathologic observations were analyzed by using Kruscall Wallis test for all histopathologic parameters and Mann-Whitney U test for variations between two groups. In statistical studies, $P<0.05$ was considered significant. In the stability studies, there were no noticeable changes in the organoleptic properties of the formulations in terms of appearance, colour and odour over the entire stability test period. In addition, measurement results of pH, viscosity and conductivity were not changed during stability studies. In the studies of excisional wound model, the percentage wound healing results gave significant changes. Due to the balsam of oriental sweet gum, Levant storax cream (LS) is more viscous than others and it has antimicrobial activity. Because of these properties, its effects on contraction of the wounds was the best among all groups (Figure 2). The complex cream (C) contains some very well recognized functional actives such as escin, *Aloe vera*, allantoin and calendula oil. All these actives bring fibroblast stimulating, anti-inflammatory and anti-oedema properties to the C which in turn resulted in statistically better contraction rates of complex cream compared to control group (Figure 2). Histopathological studies indicated that healing phase was complete for LS (Figure 3). These results indicate that histopathologically both experimental creams performed better than the reference cream, placebo cream and the control group. The studies indicated that Levant storax cream treated rats had the best healing rates compared to all the other groups, whereas the group that was treated with complex cream showed a better healing rate than control and placebo groups. However no significant difference was found between the complex and the reference groups.

Biography

Derya was studied at Yeditepe University Faculty of Pharmacy, 2003-2008. Derya got a sholarship during 2007 to 2008 at Yeditepe University and graduated from the Faculty of Pharmacy among second of seventy students. The title of graduation project was *'Resveratrol liposome incorporated into the edible film'*. She started to work as a Teaching and Research Assistant in the Pharmaceutical Technology Department at Yeditepe University Faculty of Pharmacy in 2008. In the same year, Derya was started to master programme of Cosmetology and her M.Sc. thesis entitled *'Design of New cream formulations and assessing their effectiveness on wound healing by using in-vivo animal model' u*nder the supervision of Assist. Prof. Dr. Yasemin Yağan Uzuner. Derya has completed her master degree in 2011. At the same year, she was started to Ph.D programme of Pharmaceutical Technology at Istanbul University, Faculty of Pharmacy. Derya Algül is currently employed as Research and Teaching Assistant at Yeditepe University, Department of Pharmaceutical Technology and goes on the Ph.D programme.