Original ARTICLE Mirror of Research in Veterinary Sciences and Animals MRVSA/ Open Access DOAJ

The chemical composition and effect of *Chenopodium botrys* L. Chenopodiaceae on a mouse model of excisional wound: Introducing an herbal wound dressing

Zahra Solaymanitabar; Naser Karimi, Isaac Karimi * ; Namdar Yousofvand

Department of Biology, Faculty of Science, Razi University 67149-67346, Kermanshah, Iran

ARTICLE INFO

Received: 26.02.2020
Revised: 05.03. 2020
Accepted: 15.03.2020
Publish online: 05.04.2020

***Corresponding author:**
Isaac Karimi; Email address: **isaac_karimi2000@yahoo.com.** Tel & Fax:0098-83-34274545

Abstract

This study was aimed to prepare pre-clinical evidences for wound dressing property of powder of *Chenopodium botrys L. (Chenopodiaceae)* on mouse model of excisional wound as reported in Kurdish ethnomedicine through millennia. Chemical composition of an essential oil isolated from aerial parts of *C. botrys* L. was analyzed by GC-MS. Eighteen male mice were randomly divided into three equal groups: the group receiving full wound dressing using powder (0.400 g), the group receiving partial wound dressing using powder (0.125 g) and the control group. From the first day of wound induction, the powder was daily dressed on the wounds of treated groups. The wound diameter was measured post-wounding daily and the healing process was evaluated and formulated. Among thirty-nine compounds of the essential oil of *C. botry* L. β-eudesmol (32.22%), elemol (23.35%), juniper-camphor (7.59%), cedren-9-α-ol (4.31%), α-santanol (3.76%) and myrcene (2.90%) were main sesquiterpenes. The wound closure rate showed the steepest in wounded mice received full wound dressing ($y = -1.8286x + 13.329$; $R^2 = 0.9244$) as compared to wounded mice received partial wound dressing ($y = -1.7048x + 12.671$; $R^2 = 0.9694$) and normal wounded mice which left to heal normally ($y = -1.5893x + 13.889$; $R^2 = 0.909$). However, there was not discrepancy among groups on the eighth post-wounding day which all wounds were repaired. The present study demonstrated that plant powder of *C. botrys* hastened the process of wound healing and shortened the time required for a complete wound healing.

To Cite this article: Zahra Solaymanitabar, Naser Karimi, Isaac Karimi, Namdar Yousofvand. (2020). The chemical composition and effect of *Chenopodium botrys* L. Chenopodiaceae on a mouse model of excisional wound: Introducing an herbal wound dressing. (2020). MRVSA. 9 (1): 26-36. Doi: http://dx.doi.org/10.22428/mrvsa-2020-0092-02

Keywords: *Chenopodium botrys* L., essential oil, GC-MS, wound closure rate, mice

Introduction

Chenopodium botrys L. Chenopodiaceae, is an annual or biennial herb has been used as expectorant, anticonvulsant and tonic remedy in Iranian traditional medicine (Zargari,

1993; Semnani and Semnani, 2015) while whole plant powder has been employed as herbal wound dressing in Kurdish ethnomedicine through millennia. The various extracts derived from *C. botrys* have been traditionally prescribed for catarrh and asthma, worm parasitism, pain, headache, common colds, and influenza (Semnani and Semnani, 2015). In Serbian traditional medicine, dried aerial parts of *C. botrys* were used as diuretic, antispasmodic, carminative, and antidiarrhoic remedies (Maksimović *et al.,* 2005). In Skardu valley of Pakistan, whole plant infusion is used orally for treatment of stomachache, liver complaints, and headache; it is also acknowledged as laxative and diuretic (Bano *et al.,* 2014). Young leaves and branches of *C. botrys* were used for healing of wounds in Kohistan valley, Khyber Pakhtunkhwa, Pakistan (Hazrat *et al.,* 2011).

In India, *C. botrys* is known as stimulant, diuretic, carminative, antispasmodic, and emmenagogue; it is also used in asthma, catarrh, and gastric and hepatic diseases (Semnani and Semnani, 2015). In Germany, *C. botrys* frequently cultivated against moths and used as a medicinal plant till nineteen century (Semnani and Semnani, 2015). In Spain, *C. botrys* "Valladolid tea" prescribed for coughs and probably digestive disorders or wound infestation (Pardo *et al.,* 2005).

C. botrys of different origins yielded 0.08-2% essential oil (EO) containing flavonoids, alkaloids, and several terpenoids (Semnani and Semnani, 2015; Yousef *et al.*, 2011; Chitra *et al.,* 2009; Hosamani *et al.,* 2004; Schultz, 1999; Okoli *et al.,* 2007).

In this line, bicyclic sesquiterpenoids were found in *C. botrys* (Kokanova-Nedialkova *et al.,* 2009) and its distinguishing scent is caused by monoterpenes and sesquiterpenes (Kletter and Krichbaum, 2001). The headspace of *C. botrys* contained monoterpenes including camphor, *δ*-3-carene, fenchone, linalool, menthone, nerol, *β*-pinene, pulegone, terpineol-4 and thujone and sesquiterpenes including *β*-elemene, elemol and *β*-eudesmol (Hazrat *et al.,* 2011).). Early studies on the EO of *C. botrys* mentioned to ascaridole as a bicyclic monoterpene with impressive biological activities (Kletter and Krichbaum, 2001). Iranian EO of *C. botrys* showed presence of 2,3-dehydro-4-Oxo-β-ionon, (+)-7-*epi*-amiteol, elemol, *α*-cadinol and *tau*-cadinol as main components (Mahboubi *et al.,* 2011). Moreover, in the EO of Greek *C. botrys*, sesquiterpenes including elemol acetate, elemol, botrydiol, *α*-chenopodiol, *β*-eudesmol and selina-3, 11-dien-6α-ol have been identified as major components (Tzakou *et al.,* 2007).

Kurdish ethnics used the whole plant as a wound dressing. Hence, the aim of this study was to mimic precise traditional usage of whole plant powder of *C. botrys* in experimental wound healing to provide preclinical evidence for ethnic tradition of this plant as a wound dressing matter.

Materials and Methods

Essential oil of *Chenopodium botrys* L.

The samples of *C. botrys* have been collected from Bisotun (34° 23′ N, 47° 26′ E) region of Kermanshah province and authenticated by a botanist (second author). Seventy grams of dried herb was slightly crushed and emptied into the balloon of Clevenger apparatus to drain its EO. The EO of the plant was then completely thermo-extracted for 4 to 5 hours. At the end, the EO was extracted and completely dewatered and kept in the refrigerator for phytochemical analysis.

Gas chromatography–mass spectrometry (GC-MS)

Shimadzu model GC-17A (Kyoto, Japan) gas chromatograph coupled to a Shimadzu Quadruple-MS model QP5050 mass spectrometer was employed for GC-MS analysis. Compounds were separated on a 30 m × 0.22 mm i.d. fused-silica capillary column coated with 0.25 µm film of BP-5 (Shimadzu) and a split/splitless injector with a 1mm internal diameter glass liner. Ultra-pure helium was carrier gas with ionization voltage of 70 eV. Injector and interface temperatures were 280 and 260 ◦C, respectively. Mass ranged from 35 to 450 amu and program of oven temperature was the same as abovementioned for the GC. The constituents were identified using calculation of their retention indices under temperature-programmed conditions for *n*-alkanes (C8–C20) and the oil on a DB-5 column under the same chromatographic conditions. Genotype compounds was identified in comparison to their mass spectra with those of the internal reference mass spectra library (NIST08 and Wiley 9.0).

In vivo animal model of excisional wound

Experimental design and animal maintenance were approved by ethical committee of Razi University and followed the NIH Guide for the Care and Use of Laboratory Animals. In this study, male Naval Medical Research Institute (NMRI) mice (*Mus musculus* L.; n = 18; six month-old; 20–25 g) were kept at 20 to 22 ºC in 12 hours of darkness and 12 hours of light with free access to water and feed except during induction of wound. To wound, each animal was anesthetized with ketamine and xylazine cocktail and after preparation of the skin behind neck area, a circular excisional wound was made up with scissors in sterile conditions. The depth of the wound included dermis and hypodermis and the day of surgery was considered the first day. The diameter and duration of complete wound closure were measured. The wounded animals were randomly divided into three equal groups as follows: the group (P) receiving partial wound dressing by whole plant powder (0.125 g), the group (F) receiving full wound dressing by whole plant powder (0.400 g), and the control group (C) that did not receive any treatment. From the first day after the wound induction until complete recovery, the wounds in treated groups received once-daily dressing by whole *C. botrys*. The diameter of the wound was recorded and formulated daily till full wound closure presented by zero diameter (*vide infra*).

Statistical analysis

The SPSS version 22 software for Windows (SPSS, Chicago, IL, USA) was used to analyze the data. The wound area and the percentage of wound healing in different groups and in different days were analyzed by repeated measures ANOVA and *post hoc* Tukey's HSD was employed to compare the means. A P value ≤ 0.05 was considered as significant and results were reported as mean ± standard error of the mean (SEM).

Results

Essential oil of *Chenopodium botrys* L.

The chemical composition of EO isolated from *C. botrys* were presented in Table 1 and Figure 1. Accordingly, 39 compounds have been identified in the EO of *C. botrys*. The chief components were *β*-eudmesol (32.22%), elemol (23.35%), juniper-camphor (7.59%), cedren-9-α-ol (4.31%), α-santanol (3.76%) and myrcene (2.90%).

Figure 1. GC chromatogram of the EO extracted from *Chenopodium botrys* L. in Kermanshah, Iran. The x-axis shows the retention time (min), and the y-axis shows the intensity (abundance) of the signal.

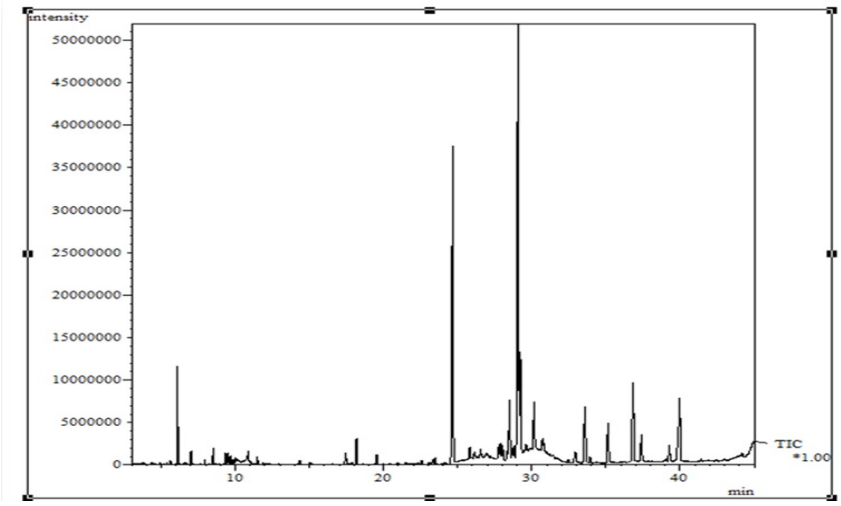

Table 1. Percentages of phytocompounds identified in essential oil of *Chenopodium botrys* L. in Kermanshah, Iran

Compound	RT	RI	KI	Similarity	Area	Area%
Hexanal	3.767	801.6	800	88%	458209	0.055597
2-Hexenal	4.358	857.9	854	90%	438150	0.055597
α-Pinene	5.367	937.8	939	90%	427589	0.055597
Camphene	5.625	955	953	89%	1084069	0.111193
Sabinene	5.967	977.8	976	88%	477863	0.055597
Myrcene	6.1	990.3	991	94%	26691673	2.909563
3-Carene	6.608	1014.8	1011	90%	998312	0.111193
p-Cymene	6.925	1030.0	1026	80%	407004	0.037064
Limonene	7.008	1034.0	1031	95%	4146566	0.444774
Cineole	7.133	1040.0	1033	80%	410152	0.037064
Terpinplene	8.217	1092.1	1088	80%	399552	0.037064
Fenchone	8.508	1104.5	1087	97%	9533824	1.037806
Cis-*β*-terpineol	9.35	1134.7	1144	89%	5116231	0.555967
Pinan-2-ol	9.508	1140.3	1142	93%	4945540	0.537435
Camphor	10.217	1165.7	1143	80%	2589124	0.277984
Menthone	10.283	1168.0	1154	80%	647294	0.074129
Isomenthol	10.858	1188.6	1182	82%	7889074	0.852483
1-Terpin-4-ol	11.017	1194.3	1177	90%	970656	0.111193
α-Terpineol	11.467	1208.6	1189	92%	4293106	0.463306
trans-Piperitol	11.867	1220.3	1205	88%	718583	0.074129

Menthyl acetate	14.342	1293.2	1275	91%	2584668	0.277984
p-Menth-1-*en*-9-ol	15.058	1312.8	1291	90%	1308326	0.148258
Terpinyl acetate	16.55	1352.2	1350	88%	618154	0.074129
Undecanol	17.433	1375.5	1372	97%	7788017	0.852483
β-Elemene	18.167	1394.9	1391	90%	14348685	1.575241
Caryophyllene	19.533	1429.7	1404	93%	5494120	0.593032
Germacrene D	21.942	1490.9	1480	80%	766905	0.092661
β-Selinene	22.558	1506.5	1485	87%	2600952	0.277984
δ-Cadinene	23.308	1525.6	1524	88%	2557690	0.277984
Elemol	24.667	1560.2	1549	90%	213716039	23.35063
Germacrene D-4-ol	25.817	1589.4	1574	95%	7948173	0.871016
Caryophyllene oxide	26.117	1597.1	1581	84%	6927454	0.759822
Guaiol	26.542	1608.0	1595	94%	10131909	1.111935
Viridiflorol	26.958	1618.8	1590	80%	6158803	0.667161
γ-Eudesmol	28.025	1646.3	1630	91%	9595564	1.056338
Cedren-9-*α*-ol	28.492	1658.4	1650	80%	39488257	4.318013
β-Eudesmol	29.067	1673.3	1658	81%	295404764	32.22758
Juniper Camphor	29.217	1677.1	1691	88%	69634512	7.598221
α-Santanol	30.142	1701.0	1678	80%	34397592	3.762046

Note: RI: retention index; KI: Kovats index; RT: retention time

The effect of *Chenopodium botrys* L. powder on skin wound healing in mice

On the first (P_{ANOVA} = 0.989; $F_{2, 14}$= 0.011), second (P_{ANOVA}= 0.567; $F_{2, 14}$=0.596), and third (P_{ANOVA}= 0.156; $F_{2, 14}$= 2.174) day of the study, there were not any differences in the diameter of wounds among groups. However, in the 4th day of study, there was a significant difference in the diameter of wounds among groups (P_{ANOVA} = 0.034; $F_{2, 14}$ = 4.542). In this day, both *C. botrys* treated groups showed similar wound diameters (P = 0.228) while diameter of wound closure was reduced significantly (P = 0.028) and non-significantly (P = 0.448) in P and F group compared to C group, respectively (Table 2). Also, in the 5th day of study, there was a significant difference among groups (P_{ANOVA} = 0.002; $F_{2, 14}$ = 10.541). In this day, P (P = 0.027) and F (P = 0.002) group showed smaller wound diameters than that of C group (Table 2) while there was no difference in wound diameters between P and F groups (P = 0.324). On 6th day of the study, there was a significant difference in wound diameters among groups (P_{ANOVA} = 0.02; $F_{2, 14}$= 5.540). In this day, P (P = 0.056) and F (P = 0.023) group showed smaller wound diameters than that of C group (Table 2) while there was no significant difference between P and F groups (P = 0.878). On 7th day of the study, there was a significant difference in wound diameters among groups (P_{ANOVA} = 0.018; $F_{2, 14}$= 5.714) among groups. In this day, P (P = 0.032) and F (P = 0.032) showed a smaller wound diameter than C group but there was no significant difference between P and F groups (P = 1.000). Finally, there was no

discrepancy among groups on 8th day of study and the wounds of all groups were completely resolved (Table 2).

Table 2. The wound dressing effect of *Chenopodium botrys* L. powder on the diameter of the skin wound (mm) in mouse model od excisional wound

Group	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8
C	10.8±2.2	10.2±1.7	9.6±1.8	9.0±1.5[a]	7.8±0.8[a]	4.4±1.5[a]	2.0±1.8	0.0±0.0
P	11.0±2.7	9.0±2.0	7.6±1.1	6.6±1.1[b]	4.6±2.0[b]	1.2±2.6[b]	0.0±0.0	0.0±0.0
F	10.8±2.2	9.8±1.4	8.6±1.5	8.0±1.0[ab]	3.0±1.8[b]	0.6±1.3[b]	0.0±0.0	0.0±0.0

NC: Control group, p: treated group with a low dose of plant powder (0.125 g), F: treated group with a high-dose plant powder (0.400 g). Values with different letters show significant difference at P value ≤ 0.05.

The Figure 2 provided an overview of wound closure rate in all groups. It showed the reliable linear relations between wound diameter (y-axis) and time (day; x-axis) with similar wound diameter in initial day (y-intercept) and various slopes (closure rates). Based on various equations depicted in Figure 2, closure rate was the steepest (-1.8286) in F group among all groups and P group also showed more closure rate (-1.7048) than C group (-1.5893).

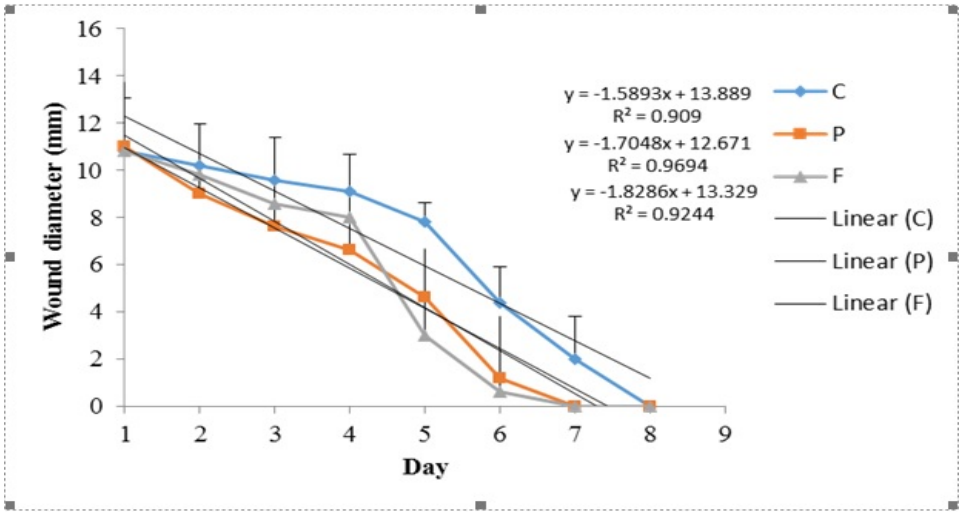

Figure 2. The effect of *Chenopodium botrys* L. powder on the closure of skin wound healing in mice.
(N = Control group, P = the treated group with low doses of plant powder (0.125 g), F = the treated group with High dose of powdered plant (0.400 g).

Discussion

Among compounds (n = 39) of EOs of *C. botrys*, *β*-eudmesol (32.22%), elemol (23.35%), juniper-camphor (7.59%), cedren-9-*α*-ol (4.31%), *α*-santanol (3.76%) and myrcene (2.90%) were detected as main components. In other study, the EO derived from aerial parts of *C. botrys* through hydro-distillation showed 29 compounds which α-oidmesol (15.2%), epi-*α*-morolol (11.1%) and cobenol (10.2%) were reported as major compounds (Rustaiyan *et al.,* 2003).). In this continuum, the EO of this plant was extracted by hexane led to identification of 19 compounds which α-chenopodiol acetate (35%) and oidesma-dien-6-*α*-ol (18.2%) were chief compounds (Rustaiyan *et al.,* 2003).). The reason for the difference in the type and amount of phytocompounds in the EOs of *C. botrys* collected from different regions can be due to the various used parts of plants, and their different climatic and geographical conditions.

Several studies have been mentioned to essential oil or extracts of herbs as wound healers in traditional medicine, however the traditional application of herbs or parts of herbs have been not reported the strict applications of the extract or EO. The EO of *C. botrys* has been studied widely and the presence of some oxygen-containing sesquiterpenes with prominent antibacterial and antifungal activities in various parts of this plant has been described (Kokanova-Nedialkova *et al.,* 2009; Yadav *et al.,* 2007; Tzakou *et al.,* 2007). For instance, the EO (0.43%w/w) isolated from aerial parts of *C. botrys* collected from southern Serbia exhibited significant bactericidal and fungicidal activity against an array of microorganisms like *Staphylococcus aureus, Bacillus subtilis, Escherichia coli, Pseudomonas aeruginosa, Aspergillus niger, Candida albicans, Sarcina lutea, Klebsiella pneumoniae, Salmonella enteritidis and Shigella flexneri* (Maksimović *et al.,* 2005). Moreover, the oil of *C. botrys* growing in Saudi Arabia showed antimicrobial activity (El-Sayed *et al.,* 1989). The results of antimicrobial activity of the EO from aerial parts of *C. botrys* growing in Greece were also reported (Tzakou *et al.,* 2007). The EO of *C. botrys* exhibited significant antibacterial activity against *Salmonella heidelberg* and *Bacillus cereus* and the residual water solution showed a good activity against *Salmonella heidelberg* and *Bacillus cereus* (Kokanova-Nedialkova *et al.,* 2009, Lyubenova *et al.,* 2006). The EO of *C. botrys* collected from suburb of Kashan, Iran showed strong antimicrobial activity against *Staphylococcus saprophyticus* followed by *Klebsiella pneumoniae, Bacillus cereus, Staphylococcus epidermidis, Streptococcus mutans, Listeria monocytogenes* and *Salmonella typhimurium* while this EO had minor effect on *Candida albicans* and showed inhibitory effect on *Aspergillus species* and *Bacillus subtilis* (El-Sayed *et al.,* 1989). More surprisingly, several species, including *C. botrys*, possess compounds that have been demonstrated to interfere with mitochondrial function (Semnani and Semnani, 2015). The wound area is very susceptible to infections caused by some abovementioned microorganism. Therefore, antimicrobial effects of various EOs derived from *C. botrys* may involve in accelerated healing process of wounds as compared to control animals. Wound is simply a loss of cellular and functional continuity of living tissue. Although the process of wound healing is natural (Chitra *et al.,* 2009).) as seen in control mice in this study, an infection can delay healing.

More specifically, one study showed that *C. botrys* L. EO improved wound healing activity in animals as a preclinical study (Sayyedrostami *et al.,* 2018). The obtained

results showed that application of *C. botrys* L. on wounds induced considerable wound contraction and accelerated healing which is in agreement with the results of the present study, so it may be a good candidate to treat different types of wounds in animals and human beings (Sayyedrostami *et al.,* 2018). In contrast to Sayyedrostami et al's study (Sayyedrostami *et al.,* 2018), which focused on wound healing of *C. botrys* L. EO, we completely translated ethnical application of *C. botrys* whole plant as wound dressing material in a mouse model of excisional wound and our findings showed that the slope of wound closure were the steepest in wounded mice that received full wound dressing by *C. botrys* ($y = -1.8286x + 13.329$; $R^2 = 0.9244$) as compared to wounded mice that received partial wound dressing by *C. botrys* ($y = -1.7048x + 12.671$; $R^2 = 0.9694$) and normal wounded mice which left to heal naturally ($y = -1.5893x + 13.889$; $R^2 = 0.909$). The overview of previous investigations focused on wound healing potentials of selected *C. botrys* terpenoids have been summarized in seminal review (Rita *et al.,* 2013). In this line, numerous medicinal properties and phytocompounds like monoterpenes, sesquiterpenes and phenolic compounds have been reported in *C. botrys*. In this essence, *β*-eudesmol as a sesquiterpene was the most abundant chemical compound found in the EO of *C. botrys* which possesses many pharmacological effects including antitumor effects (Sghaier *et al.,* 2016), although its wound healing effect has not yet been reported. Among the other chemical compounds found in *C. botrys* EOs, one may mention to limonene, *α*-pinene, 3-carene, terpineol, cineole, camphor, cryophyllene oxide and sabinene which are monoterpenoid compounds with anti-inflammatory effects (Rita *et al.,* 2013). In addition to anti-inflammatory properties, the properties of tissue repair have been reported for limonene (Rita *et al.,* 2013). Likewise, for terpineol, anti-cancer effects and wound healing have been reported (Rita *et al.,* 2013). Cineole has also been reported to be effective in the treatment of asthma and sinusitis. Caryophyllene oxide is also a monoterpene compound with anticancer and wound healing properties (Rita *et al.,* 2013). The *α*-santanol is also one of the many compounds in *C. botrys* EO which is a sesquiterpene effective in the treatment of skin diseases and skin cancer (Xiaoying *et al.,* 2010**)**. Consequently, the EOs of *C. botrys* can be effectively applied in the treatment of various maladies like tissue injuries and wounds. In conclusion , the findings of this study not only prove the ethnical usage of *C. botrys* as a wound dressing remedy but also introduce a natural herbal wound dressing matter for traumatic conditions for desert dwelling inhabitants like Kurdish people. It appears, this wound dressing remedy initially dries wound area through osmosis because of its vascular texture and then sustainably release its antimicrobial or putative mitogenic compounds that speed up the wound healing process, however more investigations are acknowledged to decipher mechanisms of wound healing of *C. botrys*.

Acknowledgements

This paper originated from MSc thesis of first author submitted to Department of Biology, Faculty of Science, Razi University 67149-67346, Kermanshah, Iran. This study was supported by intramural fund and we are pleased to thank Mrs Mohaddeseh Sayyadi Bisotuni for sharing ethnic knowledge.

Disclosure Statement

No potential conflict of interest was reported by the authors.

References

Bano A, Ahmad M, Ben H.T, Saboor A, Sultana S, Zafar M, Khan M.P, Arshad M, Ashraf M.A. (2014). Quantitative ethnomedicinal study of plants used in the Skardu valley at high altitude of Karakoram-Himalayan range, Pakistan. Journal of Ethnobiology and Ethnomedicine, 10: 43.

Chitra S, Patil M.B, Ravi K. (2009). Wound healing activity of *Hyptis suaveolens* (L) poit (Laminiaceae). International Journal of Pharmacy and Technology, 3: 737-744.

Dalazen P, Molon A, Biavatti M.W, Kreuger M.R.O. (2005). Effects of topical application of extract from *Vernonia scorpioides* on excisional wounds in mice. Brazilian Journal of Pharmacognosy, 15: 82-87.

El-Sayed A.M, Al-Yahya M.A, Hassan M.M.A. (1989). Chemical composition and antibacterial activity of the essential oil of *Chenopodium botrys* growing in Saudi Arabia. International Journal of Crude Drug Research, 27: 8-185.

Hazrat A, Nisar M, Shah J, Ahmad S. (2011). Ethnobotanical study of some elite plants belonging to Dir, Kohistan valley, Khyber Pukhtunkhwa, Pakistan, Pakistan Journal of Botany, 43: 787-95.

Houghton P.J, Hylands P.J, Mensah A.Y. (2005). *In vitro* tests and ethno pharmacological investigations: wound healing as an example. Journal of Ethnopharmacology, 100: 100–107.

Hosamani K.M, Ganjihal S.S, Chavadi D.V. (2004). *Alternanthera triandra* seed oil: A moderate source of ricinoleic acid and its possible industrial utilization. Industrial Crop Production, 19: 133-136.

Kletter C, Krichbaum M. (2001). Tibetan Medicinal Plants. Medpharm Scientific Publishers. 11: 6-241.

Kokanova-Nedialkova Z, Nedialkov P.T, Nikolov S.D. (2009). The genus Chenopodium: phytochemistry, ethnopharmacology and pharmacology. Pharmacognosy Reviews, 3: 280-306.

Mahboubi M, Ghazian Bidgoli F, Farzin N. (2011). Chemical composition and antimicrobial activity of *Chenopodium botrys* L. Essential oil, 14: 498-503.

Maksimović Z.A, Dordević S, Mraović M. (2005). Antimicrobial activity of *Chenopodium botrys* essential oil. Fitoterapia, 76: 4-112.

Nouri J, Khorasani N, Lorestani B, Karami M, Hassani A.H, Yousefi N. (2009). Accumulation of heavy metals in soil and uptake by plant species with phytoremediation potential. Environmental Earth Sciences, 59. 315-23.

Lyubenova M, Geneva Y, Chiplska L, Hadjieva P, Chanev C.H.R. (2006). Biological active components of *Chenopodium botrys* L. Phytomass. Journal of Balkan Ecology, 9: 95-289.

Okoli C.O, Akah P.A, Okoli A.S. (2007). Potentials of leaves of *Aspilia africana* (Compositae) in wound care: an experimental evaluation. BMC Complementary and Alternative Medicine, 1: 7-24.

Pardo de, Santayana M, Blanco E, Morales R. (2005). Plants known as té in Spain: an ethno-pharmaco-botanical review. Journal of Ethnopharmacology, 98: 1–19.

Rita de Cássia da Silveira e Sá, Luciana Nalone Andrade, Damião Pergentino de Sousa. (2013). A review on anti-inflammatory activity of monoterpenes. Molecules,18:1227-1254.

Rustaiyan A, Sedaghat S, Tehrani, M.S, Masudi S.H and Feizbakhsh A. (2003). Chemical composition of the essential oils of *Chenopodium botrys* L. from two different locations in Iran. Journal of Essential Oil Research, 15: 193-194.

Sayyedrostami T, Pournaghi P, Ebrahimi Vosta-Kalaee S and Zangeneh, M.M. (2018). Evaluation of the wound healing activity of *Chenopodium botrys* leaves essential oil in Rats (A Short-Term Study). Journal of Essential Oil Bearing Plants, 21: 164-174.

Schultz G.S. (1999). Molecular Regulation of Wound Healing. In: Acute and Chronic Wounds: Nursing Management, Bryant, R.A. (Ed.). 2nd Edn, WB Saunders Publisher, USA. 413-429.

Sghaier M, Mousslim M, Pagano A, Ammari Y, Luis J, Kovacic H. (2016). Beta-eudesmol, a Sesquiterpene from *Teucrium ramosissimum*, inhibits superoxide production, proliferation, adhesion and migration of human tumor cell. Environmental Toxicology and Pharmacology, 46: 227 - 233.

Semnani, K. Semnani, M. (2015). A review on *Chenopodium botrys* L.: traditional uses, chemical composition and biological activities, Pharmaceutical and Biomedical Research, 1: 1-9.

Tzakou O, Pizzimenti A, Pizzimenti F.C, Sdrafkakis V, Galati E.M. (2007). Composition and antimicrobial activity of *Chenopodium botrys* L. essential oil from Greece. Journal of Essential Oil Research, 19: 4-292.

Xiaoying Z, Wei C, Ruth G, Gudiseva Ch, Radhey S.K, Alan Y, Hesham F, Chandradhar D. (2010). Alpha-santalol, a chemopreventive agent against skin cancer, causes G2/M cell cycle arrest in both p53-mutated human epidermoid carcinoma A431 cells and p53 wild-type human melanoma UACC-62 cells. BMC Research Notes, 3: 1500-1765.

Yadav N, Vasudeva N, Singh S, Sharma S.K. (2007). Medicinal. Properties of genus *Chenopodium Linn*. Natural Product Radiance, 6: 4-131.

Yousefi N, Chehregani A, Malayeri B, Lorestani B, Cheraghi M. (2011). Investigating the effect of heavy metals on developmental stages of anther and pollen in *Chenopodium botrys* L. (Chenopodiaceae). Biological Trace Element Research, 140: 368-76.

Zargari A. (1993). Medicinal Plants. J. Tehran Univ. Publications. Tehran. Iran. 4: 9-218.