



Asian Journal of Clinical Nutrition

ISSN 1992-1470

science
alert

ANSI*net*
an open access publisher
<http://ansinet.com>

***Berberis vulgaris* Juice and Acne Vulgaris: A Placebo-Controlled Study**

Mary Johnson and Naser Rafikhah

Drug Applied Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

Corresponding Author: Naser Rafikhah, Drug Applied Research Center, Tabriz University of Medical Sciences, Medical Research and Development Complex, Daneshgah St., Tabriz, 51656-65811, Iran

ABSTRACT

It has previously shown that aqueous extract of dried *Berberis vulgaris* fruit is useful against inflamed and total acne lesions. This study aimed to investigate the role of fresh *Berberis vulgaris* fruit juice in decreasing acne lesion counts in a group of patients with mild-to-moderate acne vulgaris. A total of 38 volunteers with mild-to moderate acne vulgaris were enrolled in this study; double-blind, placebo-controlled, randomized clinical trial. They received either 100 mL freshly prepared *Berberis vulgaris* fruit juice (n = 18, case group) or placebo (n = 20, control group) once daily for 30 consecutive days. Facial acne noninflamed, inflamed and total (noninflamed plus inflamed) lesions were counted at baseline, on week 2 and at endpoint (day 30) by an observer who was not aware of the grouping of patients. In the case group, there were 9 males (50%) and 9 females (50%) with a mean age of 16.1±3.9 years (Range: 12-25). In the control group, there were 9 males (45%) and 11 females (55%) with a mean age of 15.9±4.7 years (Range: 12-29). The two groups were matched for sex (p = 0.76) and age (p = 0.89). Changes in the mean count of noninflamed lesions were not different between the two groups (p = 0.33). In contrast, the mean number of inflamed and total acne lesions decreased significantly more pronounced in the case than in the control group (p = 0.01 and 0.02, respectively). In conclusion, this study showed that fresh *Berberis vulgaris* fruit juice is effective against acne lesions in patients with mild-to-moderate disease.

Key words: Acne vulgaris, *Berberis vulgaris*, facial lesion

INTRODUCTION

Herbal remedies are getting more and more popularity in modern medicine (Azimi *et al.*, 2012; Sinha *et al.*, 2014).

Berberis vulgaris is one of those plants that are very popular in the field of herbal therapy because firstly, it is known almost all over the world and secondly many beneficial properties have been identified in extracts obtained from fruit, leaf, bark and root of this plant (Seki and Morohashi, 1993; Fouladi, 2012).

Acne vulgaris as one the most prevalent skin disease worldwide, is treated usually by using numerous synthetic medications available in the market (Babaeinejad *et al.*, 2011; Fattahi *et al.*, 2011; Fouladi, 2012, 2013; Khodaeiani *et al.*, 2012; Babaeinejad and Fouladi, 2013; Khodaeiani *et al.*, 2013). Although, many of these medications are effective, major complications are sometimes inevitable (Navali *et al.*, 2011).

Anti-microbial, anti-inflammatory and anti-oxidant properties of *Berberis vulgaris* have nominated this plant as a good herbal medication against acne vulgaris (Local Food-Nutraceuticals Consortium, 2005; Imanshahidi and Hosseinzadeh, 2008; Tomosaka *et al.*, 2008). In recent study, the extract of *Berberis* dried fruit significantly decreased inflamed and total lesion counts in a group of patients with acne vulgaris (Fouladi, 2012).

This study aimed to investigate the effect of fresh *Berberis vulgaris* fruit juice against acne vulgaris in patients with mild-to-moderate disease.

MATERIALS AND METHODS

This study was a double-blind, placebo-controlled, randomized clinical trial, carried out on 40 volunteers with moderate-to-severe acne vulgaris (Burke and Cunliffe, 1984) recruited from a private clinic from July 2013 to March 2014.

Patients with secondary acne vulgaris, hypersensitivity to *Berberis*, with other concomitant dermatologic diseases and those on known anti-acne treatments started from the previous 3 months were not enrolled.

Berberis juice was prepared from fresh fruits of *Berberis vulgaris* purchased from the local market. A skilled botanist from a local university confirmed the process of obtaining and preparing *Berberis* juice. Participants were randomly allocated to two 20-patient groups, receiving either 100 mL of the prepared juice once daily (case group) or 100 mL distilled water mixed with *Berberis* artificial flavor (the controls) for 30 consecutive days.

For the purpose of blinding, the preparations were poured in similar bottles and the two groups were labeled as "A" or "B" by a colleague who was not involved in this study.

Neither the patients nor the examiner were aware of the grouping until the study was fulfilled.

Noninflamed, inflamed and total facial acne lesions were counted at baseline, on week 2 and at the endpoint.

Within the study period, the participants were asked to not use any anti-acne therapy and all followed a conventional, similar diet.

Two patients from the case group were lost during the study period.

Statistical analysis: The SPSS software version 16.0 (SPSS Inc., IL, USA) was employed for statistical analysis. The chi-square test, independent samples t-tests and Repeated Measures Analysis (RMA) were used, where appropriate. The value of $p \leq 0.05$ were considered as significant.

RESULTS

The case group included 9 males (50%) and 9 females (50%) with a mean age of 16.1 ± 3.9 years (Range: 12-25) and the mean duration of the disease of 2.9 ± 1.7 years (Range: 1-7). The control group included 9 males (45%) and 11 females (55%) with a mean age of 15.9 ± 4.7 years (Range: 12-29) and the mean duration of the disease of 2.9 ± 1.5 years (Range: 1-6).

There was no significant difference between the two groups in terms of sex ($p = 0.76$), age ($p = 0.89$) and the duration of the disease ($p = 0.94$). Changes of the mean lesion counts during the study period are set out in Table 1. Changes in the mean count of noninflamed lesions from baseline to endpoint did not differ significantly between the two groups ($p = 0.33$).

Table 1: Mean facial acne lesions at baseline, on week 2 and at endpoint in two groups receiving either *Berberis* juice (cases) or placebo (controls)

Lesion/Time	Case (n = 18)	Control (n = 20)
Noninflamed		
Baseline	19.7±4.5 (14-29)	18.8±4.1 (14-27)
Week 2	17.6±3.8 (13-27)	18.3±3.9 (14-27)
Endpoint	15.7±5.2 (10-27)	19.3±3.6 (15-27)
Inflamed		
Baseline	22.7±2.8 (18-27)	23.5±5.3 (17-36)
Week 2	18.9±3.7 (15-27)	23.0±4.7 (14-36)
Endpoint	17.0±5.1 (9-29)	22.6±4.5 (15-33)
Total		
Baseline	42.4±4.5 (36-52)	42.3±7.2 (33-63)
Week 2	36.5±5.6 (30-51)	41.2±6.6 (31-59)
Endpoint	32.7±8.2 (21-47)	41.9±6.2 (32-57)

Data is presented as mean±standard deviation

For inflamed and total lesion in Table 1, however, the mean decrease in the count was significantly higher in the case than in the control group ($p = 0.01$ and 0.02 , respectively).

The patients in the case group reported no important complications.

DISCUSSION

In the present study, oral consumption of fresh *Berberis* fruit juice was affective against inflamed and total acne lesion counts in patients with mild-to-moderate disease. Against noninflamed lesions, however, the therapeutic effect of *Berberis* juice was not statistically significant.

In line with these findings (Fouladi, 2012) showed that aqueous extract of dried fruit of *Berberis vulgaris* was effective against acne lesions. Similar to the findings of the present study, noninflamed lesions were not significantly affected. Chemical analyses on the extracts from *Berberis vulgaris* fruit have identified various compounds such as flavonoids, isoquinoline, alkaloids, carbohydrates, vitamin, etc. (Ivanovska and Philipov, 1996; Pozniakovskii *et al.*, 2003; Imanshahidi and Hosseinzadeh, 2008).

Among these identified compounds, berberine is the most important one that is believed mediates many beneficial medical effects of this plant (Kupeli *et al.*, 2002; Yesilada and Kupeli, 2002). For example (Seki and Morohashi, 1993) showed that berberine effectively arrested the lipogenesis in hamster sebaceous glands. In addition to this finding, (Imanshahidi and Hosseinzadeh, 2008) showed that some alkaloids present in *Berberis* fruit extract have potent anti-inflammatory property, a substantial characteristic of efficacious anti-acne medications.

Other anti-acne properties of *Berberis vulgaris* are attributed to its anti-oxidant property that prevents lipid peroxidation and oxidative stress (Bowe and Logan, 2010). These beneficial effects against acne lesions are believed to be due to the presence of the phenolic compounds (Tyramine, cannabisin and lyoniresinol) in the extract of its fruit (Tomosaka *et al.*, 2008). Finally, some anxiolytic effects have been proposed in connection with *Berberis* fruit extract consumption (Peng *et al.*, 2004).

It should be noted that stress is a suspected factor in the pathogenesis of acne vulgaris that exerts its pathologic consequences through changes in the immune system of the skin and compromising the cutaneous barrier function against microorganisms (Garg *et al.*, 2001; Dhabhar, 2003; Yosipovitch *et al.*, 2007).

Overall, according to the findings of the present study, fresh *Berberis vulgaris* fruit juice, like the extract of its dried fruit, is effective against mild-to-moderate acne vulgaris and can be used as a safe alternative for chemical medications. Further studies with longer follow-ups, however, are recommended in this regard (Shakeri *et al.*, 2011a, b; Amirnia *et al.*, 2012; Feiz *et al.*, 2012; Tarzamni *et al.*, 2012; Baharivand *et al.*, 2013; Pouriesa *et al.*, 2013; Daghighi *et al.*, 2014; Sabeti *et al.*, 2013).

CONCLUSION

Fresh *Berberis vulgaris* fruit juice is effective against acne lesions in patients with mild-to-moderate disease.

REFERENCES

- Amirnia, M., E. Khodaeiani, R.F. Fouladi and A. Hashemi, 2012. Topical steroids versus PUVA therapy in moderate plaque psoriasis: A clinical trial along with cost analysis. *J. Dermatol. Treat.*, 23: 109-111.
- Azimi, H., M. Fallah-Tafti, A.A. Khakshur and M. Abdollahi, 2012. A review of phytotherapy of acne vulgaris: Perspective of new pharmacological treatments. *Fitoterapia*, 83: 1306-1317.
- Babaeinejad, S., E. Khodaeiani and R.F. Fouladi, 2011. Comparison of therapeutic effects of oral doxycycline and azithromycin in patients with moderate acne vulgaris: What is the role of age? *J. Dermatol. Treat.*, 22: 206-210.
- Babaeinejad, S.H. and R.F. Fouladi, 2013. The efficacy, safety and tolerability of adapalene versus benzoyl peroxide in the treatment of mild acne vulgaris: A randomized trial. *J. Drugs Dermatol.*, 12: 1033-1038.
- Baharivand, N., A. Mahdavi-fard and R.F. Fouladi, 2013. Intravitreal clindamycin plus dexamethasone versus classic oral therapy in toxoplasmic retinochoroiditis: A prospective randomized clinical trial. *Int. Ophthalmol.*, 33: 39-46.
- Bowe, W.P. and A.C. Logan, 2010. Clinical implications of lipid peroxidation in acne vulgaris: Old wine in new bottles. *Lipids Health Dis.*, Vol. 9. 10.1186/1476-511X-9-141
- Burke, B.M. and W.J. Cunliffe, 1984. The assessment of acne vulgaris-the leeds technique. *Br. J. Dermatol.*, 111: 83-92.
- Daghighi, M.H., M. Pouriesa, M. Maleki, D.F. Fouladi, M.Z. Pezeshki, R.M. Khameneh and A.M. Bazzazi, 2014. Migration patterns of herniated disc fragments: A study on 1,020 patients with extruded lumbar disc herniation. *Spine J.*, 14: 1970-1977.
- Dhabhar, F.S., 2003. Stress, leukocyte trafficking and the augmentation of skin immune function. *Ann. N.Y. Acad. Sci.*, 992: 205-217.
- Fattahi, E., M.H. Somi, M.R. Moosapour and R.F. Fouladi, 2011. Independent predictors of in-hospital re-bleeding, need of operation and mortality in acute upper gastrointestinal bleeding. *Pak. J. Biol. Sci.*, 14: 849-853.
- Feiz, H.H., A. Afrasiabi, R. Parvizi, A. Safarpour and R.F. Fouladi, 2012. Scoliosis after thoracotomy/sternotomy in children with congenital heart disease. *Indian J. Orthop.*, 46: 77-80.

- Fouladi, R.F., 2012. Aqueous extract of dried fruit of *Berberis vulgaris* L. in acne vulgaris, a clinical trial. J. Diet. Suppl., 9: 253-261.
- Fouladi, R.F., 2013. A single case report using an antiacne topical medication for severe foot odor. JAMA Dermatol., 149: 250-251.
- Garg, A., M.M. Chren, L.P. Sands, M.S. Matsui, K.D. Marenus, K.R. Feingold and P.M. Elias, 2001. Psychological stress perturbs epidermal permeability barrier homeostasis: Implications for the pathogenesis of stress-associated skin disorders. Arch. Dermatol., 137: 53-59.
- Imanshahidi, M. and H. Hosseinzadeh, 2008. Pharmacological and therapeutic effects of *Berberis vulgaris* and its active constituent, berberine. Phytother. Res., 22: 999-1012.
- Ivanovska, N. and S. Philipov, 1996. Study on the anti-inflammatory action of *Berberis vulgaris* root extract, alkaloid fractions and pure alkaloids. Int. J. Immunopharmacol., 18: 553-561.
- Khodaeiani, E., R.F Fouladi, N. Yousefi, M. Amirnia, S. Babaeinejad and J. Shokri, 2012. Efficacy of 2% metronidazole gel in moderate acne vulgaris. Indian J. Dermatol., 57: 279-281.
- Khodaeiani, E., R.F. Fouladi, M. Amirnia, M. Saeidi and E.R. Karimi, 2013. Topical 4% nicotinamide vs. 1% clindamycin in moderate inflammatory acne vulgaris. Int. J. Dermatol., 52: 999-1004.
- Kupeli, E., M. Kosar, E. Yesilada and K.H.C. Baser, 2002. A comparative study on the anti-inflammatory, antinociceptive and antipyretic effects of isoquinoline alkaloids from the roots of *Turkish berberis* species. Life Sci., 72: 645-657.
- Local Food-Nutraceuticals Consortium, 2005. Understanding local Mediterranean diets: A multidisciplinary pharmacological and ethnobotanical approach. Pharmacol. Res., 52: 353-366.
- Navali, N., S. Pourabolghasem, R.F. Fouladi and M.A. Nikpour, 2011. Therapeutic effects of biguanide vs. statin in polycystic ovary syndrome: A randomized clinical trial. Pak. J. Biol. Sci., 14: 658-663.
- Peng, W.H., C.R. Wu, C.S. Chen, C.F. Chen, Z.C. Leu and M.T. Hsieh, 2004. Anxiolytic effect of berberine on exploratory activity of the mouse in two experimental anxiety models: Interaction with drugs acting at 5-HT receptors. Life Sci., 75: 2451-2462.
- Pouriesa, M., R.F. Fouladi and S. Mesbahi, 2013. Disproportion of end plates and the lumbar intervertebral disc herniation. Spine J., 13: 402-407.
- Pozniakovskii, V.M., O.V. Golub, D.G. Popova and I.N. Kovalevskaia, 2003. [The use of barberry berries in human nutrition]. Voprosy Pitaniia, 72: 46-49 (In Russian).
- Sabeti, S., F. Malekzad, M. Ashayer, R.F. Fouladi, K.K. Hesari, M.P. Toutkaboni and S. Younespour, 2013. The rate and pattern of bcl-2 and cytokeratin 15 expression in trichoepithelioma and nodular basal cell carcinoma: A comparative study. Indian J. Dermatol., 58: 331-336.
- Seki, T. and M. Morohashi, 1993. Effect of some alkaloids, flavonoids and triterpenoids, contents of Japanese-Chinese traditional herbal medicines, on the lipogenesis of sebaceous glands. Skin Pharmacol. Physiol., 6: 56-60.
- Shakeri, A., M. Abdi, H.T. Khosroshahi and R.F. Fouladi, 2011a. Common carotid artery intima-media thickness and atherosclerotic plaques in carotid bulb in patients with chronic kidney disease on hemodialysis: A case-control study. Pak. J. Biol. Sci., 14: 844-848.
- Shakeri, A., M.B. Bazzaz, A. Khabbazi and R.F. Fouladi, 2011b. Common carotid intima-media thickness in patients with late rheumatoid arthritis: What is the role of gender? Pak. J. Biol. Sci., 14: 812-816.

- Sinha, P., S. Srivastava, N. Mishra and N.P. Yadav, 2014. New perspectives on antiacne plant drugs: Contribution to modern therapeutics. *BioMed Res. Int.*, 10.1155/2014/301304
- Tarzamni, M.K., N. Eshraghi, R.F. Fouladi, A. Afrasiabi, M. Halimi and A. Azarvan, 2012. Atherosclerotic changes in common carotid artery, common femoral artery and ascending aorta/aortic arch in candidates for coronary artery bypass graft surgery. *Angiology*, 63: 622-629.
- Tomosaka, H., Y.W. Chin, A.A. Salim, W.J. Keller, H. Chai and A.D. Kinghorn, 2008. Antioxidant and cytoprotective compounds from *Berberis vulgaris* (barberry). *Phytother. Res.*, 22: 979-981.
- Yesilada, E. and E. Kupeli, 2002. *Berberis crataegina* DC. root exhibits potent anti-inflammatory, analgesic and febrifuge effects in mice and rats. *J. Ethnopharmacol.*, 79: 237-248.
- Yosipovitch, G., M. Tang, A.G. Dawn, M. Chen, C.L. Goh, Y.H. Chan and L.F. Seng, 2007. Study of psychological stress, sebum production and acne vulgaris in adolescents. *Acta Dermato-Venereologica*, 87: 135-139.