

A preliminary study on the efficacy of *Nerium oleander* L. extract on clinical symptoms in patients with knee osteoarthritis

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ABSTRACT

*Knee osteoarthritis is the most common joint disease in humans. Nowadays, due to common side effects of oral painkillers, topical medication have been attracted many attentions. According to authoritative source of Iranian traditional medicine, the aim of this study is the evaluation of the efficacy of *Nerium oleander* L. extract as a topical treatment of knee pain. In this study, 18 patients aged between 40 to 80 years old, who suffered from knee osteoarthritis were selected based on symptoms and radiographic findings. According to valid resources of traditional medicine, Defli plant (*Nerium oleander* L.) was selected and after extraction, the patients received topical gel three times a day for a total three weeks. The effect of drug was evaluated based on WOMAC questionnaire, visual analog scale(VAS) and global patient assessment (GPA). Eighteen patients with mean age of 59 years old participate in this study. According to results, patients who were treated with Defli gel for three weeks had significantly less pain and stiffness($p=0.00$). Physical function improvement and total score of the questionnaire after three weeks were significant ($P=0.00$). VAS showed significant difference in patient who were treated with Defli gel after treatment ($p=0.000$).Based on GPA, the recovery rate was between 10% to 80%, and its mean value was 39%. The result of our study showed that Defli gel could be effective in treating pain, stiffness and improving the quality of life in patients suffering from knee osteoarthritis in 3 weeks. According to this preliminary study, a randomized clinical trials is recommended.*

Key words: Knee osteoarthritis, *Nerium oleander* L., Pain, Physical function, Defli gel

INTRODUCTION

Musculoskeletal pains affected about one-third to one-half of the population in the world [1]. In addition, osteoarthritis is the most common joint disorder and the most common cause of disability and pain in elderly people. Incidences of osteoarthritis increase with age and obesity [2]. Prevalence of symptomatic osteoarthritis is more

important on the aspect of clinical practice and health community. Pain in the joint is the most common symptom of OA. The aim of treatment of osteoarthritis was to reduce pain and to decrease the loss of physical function. Patients with mild to intermediate pain may need only non-pharmacologic treatment, although patients with persistent pain and disability need both drug and non-drug treatment. Moreover, non-drug approach is the main treatment of OA; drugs have an important role in the adjuvant treatment of patients. Available drugs are divided to oral, topical and intra articular injection. Non-steroidal anti-inflammation drugs are the most known analgesic medication in treatment of osteoarthritis, which have many side effects. Therefore, topical medication is nowadays used widely for treatment of different diseases [3]. Concerns about the use of chemical drugs for treating health problems, especially in chronic diseases such as knee osteoarthritis, there has been increased global interest in traditional medicine. There are a lot of plants that are known in treatment of joint disorder with anti-inflammatory and painkilling effects [4]. According to this subject, evaluation of therapeutic effects of these plants is reasonable. Based on the definition of Iranian traditional scholar, joint pain is a painful condition which happened in the joints. Therefore, if the pain was not related to limb, and it is occurred in the finger and toe was named Vajaolmafasel [5]. In addition, if the joint pain affected single and particular limb, it would be specific like. If it occurred in hip joint, it would be called Vajaolvarak [6], and if the pain occurred in knees that would be named Vajaorrakbe [7]. Considering to this appellation, knee osteoarthritis will be a chronic Vajaorrakbe and Pain is a major health problem in patients with arthritis. . In this study, we assessed all of single anti-inflammation plants affecting the joints and the plant was selected on the basis of its analgesic properties. *Nerium oleander* L., which is known as Defli in traditional medicine, is a medicinal plant that effects on chronic back pain and knee pain [8,9,10,11]. Leaves of Defli in the form of plaster are an effective herbal remedy for treating back pain and knee pain [12]. According to Davood Antaki, oil of Defli could eradicate hemorrhoid, reduce the joint pain, sciatica and gout[13]. Avicenna in his book, The Canon of Medicine, has described Defli and its herbal properties. He has pointed that ,Defli is strongly dissolvent and very suitable for treating itches, scabies and exfoliation and use of its leaves oil is effective in chronic back ache and knee pain [14]. Defli is a strong dissolvent and has a beneficial effect on hard swelling, itching, scabies, backache and knee pain especially when is used in the form of plaster [15]. Defli is recommended to be used only topically in treatment of joint disorder especially for knee and back pain [16]. Defli is very popular and if it is used topically as a plaster, it will be a powerful dissolvent and will have an analgesic role in the treatment of back pain and knee pain [17]. In Exir-Azam, one of the most famous treatment book in Iranian traditional medicine ,is mentioned that Defli is effective in treatment of knee pain caused by coldness and it is more effective to use as combination boiled leaves of Defli and heated oils[18]. In a study in India conducted by Kumar, it was demonstrated that anti-inflammation and anti-fever properties of Defli was as effective as paracetamol[19]. Defli also showed anti-tumor effects on patients who suffer from refractory solid tumors in phase I trial. After intramuscular injection of Defli extract ,the anti-tumor effect was proved [20]. Regarding to the majority of traditional books related to treatment of Defli on chronic backache, knee pain and new research based on Defli' properties, this paper focuses on designing new formulation of Defli oil as a topical drug.

MATERIALS AND METHODS

In this study, 18 patients who suffered from knee osteoarthritis was selected based on symptoms and radiographic finding. The patients were informed of the study and all details related to knee osteoarthritis. Then, signed informed consent was obtained from all patients. Pain, stiffness and physical function was evaluated by an interview, WOMAC questionnaire and visual analog scale of pain (VAS). The results of the patients who treated with topical Defli gel was analyzed by SPSS software (version20) before and after treatment. For the extraction of Defli, fresh aerial parts of the Defli herb were selected. The plant was scientifically identified and recorded in the school of pharmacy, Shahid Beheshti University of Medical Sciences, by voucher number of 8055. The extraction of Defli leaves was prepared as a topical gel and necessary training was given to patients. They had to use topical gel three times in a day during 3 weeks. The pain, stiffness , physical function and visual analog scale of pain were evaluated before and after treatment.

RESULTS

According to the results, the mean age of patients was 59 years old. The results showed that pain and stiffness is decreased significantly by topical treatment and physical function is improved significantly [Table 1].

Table1. Comparison of three factor (pain, stiffness and Physical function) in patients pre and post of treatment with Defli gel

	Number	Min	Max	Mean	Sig(2-tailed)
Pain (before)	18	6.00	17.00	12.0000	0.000
Pain(after)	18	.00	9.00	5.3333	
Stiffness(before)	18	1.00	6.00	4.1111	0.000
Stiffness (after)	18	1.00	3.00	1.8889	
Physical function(before)	18	26.00	53.00	42.6667	0.000
Physical function(after)	18	8.00	37.00	22.3889	
Total(before)	18	36.00	75.00	62.1111	0.000
Total(after)	18	9.00	47.00	30.2778	

Visual analog scale of pain, in all of patients was evaluated before and after the treatment which was significant statistically [Table 2].

Table 2. The Visual Analog Scale (VAS) of pain in patients before and after treatment with Defli gel

	Number	Min	Max	Mean	Sig(2-tailed)
VAS before	18	3.00	8.00	6.3333	0.000
VAS after	18	1.00	6.00	3.661	

The recovery scale after treatment was assessed based on global patient assessment (GPA) and its rate was between 10% to 80% and the mean value was 39% [Table 3].

Table 3. Global Patient Assessment (GPA) of patients after treatment by Defli gel

	Number	Min	Max	Mean
GPA	18	10%	80%	39.7222

DISCUSSION

Osteoarthritis is the most common joint disorder in the world and knee arthritis is the most frequent joint disorder in Iran [21]. There are different kinds of drugs for treatment of osteoarthritis, and oral NSAIDs are the most famous drugs to treat osteoarthritic pain which have common side effects such as upper GI toxicity, increased risk of cardiovascular events, blood pressure and tendency to develop edema [3]. Because of these problems and insufficient effect of supplements such as Glucosamins [22], topical drugs have been considered for treatment. FDA has approved the use of topical NSAIDs in the treatment of osteoarthritis. Unfortunately topical NSAIDs often cause irritation, but have fewer gastrointestinal and systemic side effects [22]. Failure to complete cure by chemical drugs especially in chronic diseases, increases the need for traditional medicine drugs with anti-inflammation and analgesic effects such as capsaicin [23] and Devils Claw [24]. In Iranian traditional medicine, there are many different plants to treat joint disorder. On the bases of authoritative source of Iranian traditional medicine, *Nerium oleander* L. (Defli) was selected for further evaluation in this study. As mentioned previously, Defli is a strong dissolvent and can be effective in treatment of chronic back pain and knee pain [8,18]. In a study in Turkey, anti-inflammation and antinociceptive activity of seven different traditional plants was confirmed on animals and anti-inflammation and analgesic effect of Defli was proved. [25]. Another study was conducted on antimicrobial effects of leaves of Defli on *Bacillus pumillus*, *Bacillus subtilus*, *Staphylococcus Aureus*, *Aspergillus niger*, *Escherichia coli* and its antimicrobial property was equal with standard antibiotics [26]. Another study conducted in the United States has been showed that the extraction of Defli decrease viral infection of HIV virus from infected cells [27]. Another survey in Turkey demonstrated that the extraction of Defli is effective on fatty acid and blood sugar level of diabetic mouse and in this way; new approach was introduced in control of fatty acid and blood sugar in type II diabetes [28]. Also in recent research, *Nerium Oleander* L. is known as a plant with anti-inflammation, anti-microbial, anticancer and antinociceptive effect (19,20). Regarding to the majority of traditional books related to therapeutic effect of Defli on chronic knee pain and new research on properties of Defli, this preliminary study was designed. After preparation of Defli gel and selection of patients with knee osteoarthritis, the pain, stiffness and physical function of these patients was evaluated before and after treatment by WOMAC questionnaire and visual

analog scale(VAS).Our study showed that Defli gel can reduce pain, stiffness and can improve physical function of patients with knee osteoarthritis and base on global patient assessment (GPA), patients were satisfied by local treatment of Defli gel. This study would be an acceptable model to perform a randomized clinical trials.

CONCLUSION

According to this study, *Nerium oleander* L. extract (Defli gel) has effective impact on reduction of pain and stiffness of knee and improvement of physical function of patients with knee osteoarthritis .So a randomized clinical trial is recommended to evaluate the benefits and side effects of *Nerium oleander* L.

REFERENCES

- [1] G. Firestein, R. Budd, Sh. Gabriel, I. Mcinnes, J. Odell, S. Kelley; Textbook of Rheumatology, Elsevier Sanders, **2012**.
- [2] D.T. Felson, Y. Zhong, *Arthritis.*, **1998**, 41, 1343-1355.
- [3] A. Fauci, E. Braunward, D. Kasper, S. Hauser, D.longo, J. Jameson, J. Losalzo; Harrisons Principal of Internal Medicine, **2012**.
- [4] M.Shams ardakani, F. Farjadmand; General Guidline for methodologies on research and evaluation of traditional medicine, Shahid Beheshti University, **2006**.
- [5] R. Choopany, M. Emtiaay, M. Tnsaz, M. Khodadoust; Diagnosis of diseases in Iranian traditional medicine, Fraz andyhsabz, **2009**.
- [6] M. Arzany ;Mizanalteb, editing and research H.Nasiri, Institute of Natural Ahya'teb, **2008**.
- [7] M.Chashty ; Romuze Azam, Institute of Historical Studies, Islamic and Complementary Medicine, **2005**.
- [8] H.Avicenna; Canon of Medicine, editing and research,E. Shamsoddin, Institute Alalmy Library, **2005**.
- [9] M. Razi; Alhavy ,editing and research N. Afsharipur, Iranian Academy of Medical Sciences, **2005**.
- [10] E. Soveidi; Tazkera- Soveisdi ,translated by R. Tafaghod , Andisheavaran publications, **2011**.
- [11] M. Moemen Tonekaboni ;Tohfamol-Moemenin, Shahid Beheshti University of Medical Sciences, **2007**.
- [12] A. Heravi; edited by A. Bahmanyar, H. Mahbubi,Tehran university publications, **2010**.
- [13] D. Antaki;Tazkera, editing and research M. Mohammad, Daralebrahim, **2010**.
- [14] H. Avicenna; Canon of Medicine, Hamdard publications, **1998**.
- [15] A. Ansari Shirazi; Ekhtiarat e Badiiee, Pakhshe Razi Companies, **1992**.
- [16] M. Aghili Khorasani; Makhzan-al- advyeh, correcting and research M. Shams Ardakrni, Tehran University publications, **2010**.
- [17] Z. IbnBitar; The Whole Vocabulary of Medicine and Food, Scientific Book House, **2001**.
- [18] M. Chashty; Eksire Azam, Institute of Historical Studies, Islamic and Complementary Medicine, **1995**.
- [19] S. Kumar, R. Ganeshan, A. Reddy, A.P. Guntur, *Pharmacia.*, **2010**, 1, 33-36.
- [20] T. Mekhail, H. Kaur, R. Ganapathi, P. Elson, R.M. Bukowski, *Invest New Drugs*, **2006**, 24, 423.
- [21] F. Davatchi, A.T. Banihashemi, J. Gholami, *Clinical Rheumatology*, **2009**, 28, 1267-1274
- [22] R. Hughes, A.Carr, *Rheumatology.*, **2002**, 41, 279-284.
- [23] C.I. Dea, T.J. Schnitzer, E. Lipsteain, J.R. Seibold, R.M. Stevens, M.D. Levy, D. Albert, *Clinical Therapeutics.*, **1991**, 13, 383.
- [24] S. Chrubasic, S. Pollak, A. Black, *Rheumatology.*, **2002**, 41, 1332-1333.
- [25] N. Erdemoglu, E. Küpeli, E. Yeşilada, *Journal of Ethnopharmacology.*, **2003**, 89, 123-129.
- [26] M.A. Hussain, M. Gors, *Asian Journal of Plant Sciences.*, **2004**, 3, 177-180.
- [27] S. Singh, S. Shenoy, P.N. Nehet, P. Yang, B. Nehet, R.N. Newman, K.J. Sastry, D. Fontenot, *Fitote.*, **2012**, 10, 17.
- [28] A.L. Bas, S. Demirci, N. Yazihan, K. Uney, E. Ermis kaya., *Int J Endocrinol.*, **2012**, 10, 1155.