



Available online through

www.jbsoweb.com

ISSN 2321 - 6328

## Review Article

### PLANTAR IONTOPHORESIS WITH AQUEOUS SOLUTION OF GUGGULU IN THE MANAGEMENT OF PLANTAR FASCIITIS: ENGENDERING AN INCIPIENT DIMENSION IN ITS MANAGEMENT

Narinder Singh \*<sup>1</sup>, Ashok Kumar <sup>1</sup>, Alpona Ray <sup>2</sup>, Alok Kumar <sup>3</sup>

<sup>1</sup>Assistant Professor, P.G. Department of Shalya Tantra, National Institutes of Ayurveda, Jaipur, Rajasthan, India

<sup>2</sup>P.G. Scholar, P.G. Department of Shalya Tantra, National Institutes of Ayurveda, Jaipur, Rajasthan, India

<sup>3</sup>Ph.D. Scholar, P.G. Department of Shalya Tantra, National Institutes of Ayurveda, Jaipur, Rajasthan, India

\*Corresponding Author Email: narinder.1973@gmail.com

Article Received on: 02/01/15 Accepted on: 07/03/16

**DOI: 10.7897/2321-6328.0416**

#### ABSTRACT

Guggulu, a resin from *Commiphora mukul* is an established anti-inflammatory agent since ancient time. It has been first described in Atharva Veda in 2000 B.C. Guggulu is the dry gum resin obtained from the bark of the *Commiphora mukul*. Phyto-chemically it is found to be mixture of diterpenes, sterols, steroids, esters and higher alcohols. Topical application of Guggulu resin as anti-inflammatory agents at the site of inflammation is a proven effective measure for the arthropathies & various other musculo-skeletal conditions. Since most of the drugs showed less than adequate skin permeability, so the iontophoresis an "electrically-assisted trans-dermal drug delivery system" was proposed to be a physical technique for enhancement of skin permeation of topical drugs. Plantar fasciitis is a common cause of heel pain in adults with the peak incidence occurring in people between the ages of 40 – 60 years. Various treatment modalities have been proposed but with debatable outcome. So an effort has been made to execute plantar iontophoresis using aqueous solution of Guggulu resin in the management of plantar fasciitis.

**Key words:** Guggulu resin, *Commiphora mukul*, iontophoresis, plantar fasciitis.

#### INTRODUCTION

Plantar fasciitis is a common cause of heel pain in adults with the peak incidence occurring in people between the ages of 40 – 60yrs as stated by Harrison. 70% of patients presents with unilateral heel pain. Heel pain is a common presenting complaint in the foot and ankle practice, and plantar fasciitis (PF) is the most common cause of chronic pain beneath the heel in adults<sup>1</sup>, making up 11–15% of the foot symptoms requiring professional care<sup>2</sup> among adults. PF, which is more common in middle-aged obese females and young male athletes, has a higher incidence in the athletic population though not all suffering requires medical treatment. In the literature, PF has been described as painful heel syndrome, chronic plantar heel pain, heel spur syndrome, runner's heel, and calcaneal periostitis.

Despite the high prevalence of PF, information about its pathogenesis is still limited, and its histological changes are suggestive of degeneration rather than inflammation<sup>3</sup>. The fascia is usually markedly thickened and gritty. These pathological changes are more consistent with fasciosis (degenerative process) than fasciitis (inflammatory process), but fasciitis remains the accepted description in the literature<sup>4</sup>.

#### Clinical Features

The patient complains of pain in the medial side of the heel, most noticeable with initial steps after a period of inactivity and usually lessens with increasing level of activity during the day. It will tend to worsen toward the end of the day. Symptoms may become worse following prolonged weight bearing, and often precipitated by increase in weight bearing activities PF is

usually unilateral, but up to 30% of cases have a bilateral presentation<sup>5</sup> Tightness of Achilles tendon is found in almost 80% of cases. Occasionally the pain may spread to the whole of the foot including the toes. Tenderness can be elicited over the medial calcaneal tuberosity and may exaggerate on dorsi-flexion of the toes or standing tip toe. The clinical course for most patients is resolution of symptoms within a year.

Most of the conditions of painful heel can be understood under the term Vatakantaka (Padakantaka) in the Ayurvedic literature- It is primarily recognized as VataVyadhi, characterized by pain "as it pricked by thorns (kantaka)" in the foot (Pada) and hence the name.

#### Management

Plantar fasciitis is usually a self limiting condition. However, the typical resolution time is anywhere from 6 to 18 months or longer, which can lead to dissatisfaction of patient and physician<sup>6</sup>. Most experts agree that early recognition and management<sup>7</sup> of PF leads to short course of treatment and greater chance of success with conservative therapies.

As per principles of ayurveda local snehana, upanahaa, agnikarma, raktamokshana, bandhana, unmardana and oral administration of Eranda taila are the classical line of treatment for vatakantaka. As per the contemporary science numerous treatment modalities<sup>8</sup> have been described for treatment of PF, which include: rest, heat, ice pack, non-steroidal anti-inflammatory drugs (NSAID's), heel pads, magnetic insole, night splints, walking cast, taping, plantar and Achilles stretching, ultrasound, steroid injection<sup>9</sup>, extra-corporeal shock wave therapy, platelet-rich plasma injection, pulsed radiofrequency electromagnetic field therapy, and surgery<sup>10</sup>.

Despite evolving treatment modalities, effectiveness of any individualized therapeutic modality in reducing pain in Plantar-fasciitis is still questionable. In the current scenario there is a huge concern about the acceptability of traditional Agnikarma. Now a day the traditional Agnikarma in the management of plantar fasciitis is not a well-accepted treatment modality. Plantar Iontophoresis is a technique which involves applying anti-inflammatory substances topically to the plantar fascia and transmitting these substances through the skin with an electrical current. Iontophoresis is a physical process in which ions flow diffusively in a medium driven by an applied electric field. Plantar Iontophoresis with Aqueous solution of Guggulu resin may be an effective alternate for the management of plantar fasciitis.

### Guggulu

The noun Guggulu is coined on account of its activity against Vatavyadhi (disorder due to vitiation of Vata dosha and its ability to combat with diseases. It is a resin obtained from *Commiphora mukul*, a small shrub like tree, with thorny branches. The English name for this is Indian Bedellium. In Hindi and Sanskrit it is known as Guggulu or Guggulu This plant of family "Burseriaceae". is found extensively in the dry regions of the Indian subcontinent, mainly India, Pakistan and Bangladesh<sup>11</sup>.

### Guggulu resin

The balsam or Guggulu (oleo-gum-resin) is present in "Balsam canals" in the phloem of the larger veins of the leaf and in the soft base of the stem. Resin is tapped by incisions during months of February to June in plants over 5 years of age with a basal diameter greater than 7.5 cm<sup>12</sup>. The fragrant yellow latex oozes out through the incisions and slowly solidifies into vermicular or stalactites, which can be collected manually. About 200 to 500 g of Guggulu resin is obtained from a typical plant in one season. Snigdha (oily), picchila (sticky), madhur gandhi (having pleasant odour), tikta (bitter taste), Pitabha (yellowish tinge), water dissolving tendency are the properties of grahya Guggulu (Acceptable Guggulu).

### Bioactive compounds of Guggulu resin

The oleo-gum-resin of the Guggulu tree is a very complex mixture of gum, minerals, essential oils, terpenes, sterols, ferrulates, flavanoides, sterones and several other unknown compounds. Some bioactive compounds has been extracted from *C. mukul* are dimyrcene,  $\alpha$ -camphorene, linoleic, oleic, stearic, palmitic acids, sitosterol, Z- and E-Guggulusterones, (8R)-3 $\alpha$ ,8-dihydroxy-polypoda-13E,17E,21-triene (myrrhanolC),4-pregnene-3,16-dione;20S-acetyloxy-4-pregnene-3,16-dione; 4,17(20)-(cis)-pregnadiene-3,16-dione; 4,17(20)-(trans)-pregnadiene-3,16-dione; 16  $\beta$ -acetyloxy-pregn-4,17(20)-trans-dien-3-one; 3  $\alpha$ -acetyloxy-5 $\alpha$ -pregnan-16-one; 20R,22R-dihydroxycholest-4-en-3-one and Amino acids cystine, histidine, alanine, proline, tyrosine, tryptophan, valine, leucine and isoleucine.

### Anti-inflammatory and analgesic bio-active compound

Guggulusterone: The ole-gum-resin of *C. Mukul* is called guggulipid. Guggulusterone is a potent inhibitor NF- $\kappa$ B, COX-2 and MMP-9<sup>13</sup>. Guggulusterones also appear to reduce circulating levels of pro-inflammatory cytokines and markers such as IL-1b, IL-2 and TNF- $\alpha$ . and reduce Cyclooxygenase-2

(COX-2) mRNA levels and suppress its TNFa mediated induction (activation).

Naringenin: Naringenin is a flavonoid which shows anti-inflammatory, antihistaminic, antibacterial and antiviral properties<sup>14</sup>.

Myrrhanol A: Myrrhanol A, a triterpene of *Commiphora mukul* gum resin is recognised as potent anti-inflammatory effects<sup>15</sup>.

Myrrhanols B, myrrhanones A, myrrhanones B: These are absolute stereo structures of polypodane- and octanodammarane-type triterpenes with a potent inhibitory effects on nitric oxide production<sup>16</sup>.

Diayangambin: Diayangambin have immune-modulatory and anti-inflammatory effect and inhibit Human mononuclear cell proliferation<sup>17</sup>.

Quercetin: It has inhibitory effect on the nitric oxide pathway, have anti-inflammatory activity, possibly due to an influence on the production of eicosanoids, including leukotrienes and prostaglandins and also cytokines. Quercetin can inhibit various cytokines, including tumour necrosis factor  $\beta$  (TNF $\beta$ )<sup>18</sup>.

1, 8-cineole: 1,8 -cineole is a terpenoid oxide is an essential oil having inhibitory effect on some types of experimental inflammation and also inhibits capillary permeability<sup>19</sup>.

$\beta$ -sitosterol has been reported that it has in-vivo topical anti-inflammatory properties in acute inflammation, but not in the chronic one<sup>20</sup>.

Sitosterol and Stigmasterol: A mixture of stigmasterol and sitosterol are shown to possess anti-inflammatory activity after topical application. Mansumbinoic acid and Mansumbinone: Researches on anti-inflammatory activity of *C. Mukul* observed that two octanodammarane triterpenes and mansumbinoic acid mansumbinone exhibited significant anti-inflammatory activity<sup>21</sup>.

### What is iontophoresis

Iontophoresis is a process that allows increased penetration of ionized molecule across or into the tissue by application of low electric current. Today, the treatment of hyper hydrosis is the most successful and popular applications of iontophoresis in dermatological medication. The trans-dermal drug delivery system holds the promise that compounds could be delivered in a more effective method for the better outcome in topical applications.

Iontophoresis enhances drug delivery across the skin by three principal mechanisms:

- Iontophoresis (electro-repulsion, electro-migration or Nernst plank effect)
- Electro-osmotic flow
- Damage effect (current induced increase in skin permeation)

Electro-repulsion is the direct effect of the applied electric field on a charged permeant say drug intervened. The second mechanism, electro-osmosis, results from the fact that the skin supports a net negative charge at physiological pH, like charges repel each other, hence the charged ion is repelled by a similarly charged electrode and absorbed through the skin. The skin being negatively charged at physiological pH acts as a cation selective membrane and favours movement of cat-ions through anodal iontophoresis. Anodal iontophoresis also causes convective motion of the solvent occurring in response to movement of counter ions. This process of electro-osmosis is involved in the motion of neutral compounds as well as positively charged ions. Moreover, the injury caused by the electric current directly itself and due to the change of the ph of the skin also reduces the barrier power of the skin and increases the permeability of the larger molecules.

### Iontophoresis as drug delivery module

The potential of this technique has been exploited for the transdermal delivery of many drugs with poor penetration properties e.g., high molecular weight electrolytes such as proteins, peptides and oligo-nucleotides which are normally difficult to administer except through parenteral route. It also offers a great potential for the delivery of charged peptides used as drugs.

### Process to constitute aqueous solution of Guggulu resin

In this process, 200 gm of drug sample is boiled in 800 ml of distilled water till it dissolve. After this the solution is cooled & filtered with filter paper. This procedure is suitable for extracting water-soluble, heat stable constituents.

### Methodology

Plantar Iontophoresis with Aqueous solution of Guggulu resin on the plantar aspect have been applied. Total Six sittings (20

minute each) thrice a week on alternate days for a fortnight had been performed. The progress was noted in the specially prepared case sheet. The observations when analyzed on the basis of assessment parameters on 1<sup>st</sup> day, 7<sup>th</sup> day and 14<sup>th</sup> day revealed promising results. Keeping in view the outcomes a planned study with standard protocol has been planned with results awaited.

### CONCLUSION

Plantar fasciitis<sup>22</sup> is a commonly encountered poorly understood orthopedic complaint related to foot, associated with significant morbidity, requiring professional care. Now a day the traditional Agnikarma in the management of plantar fasciitis is not a well-accepted treatment modality. As far as contemporary science is concerned local injections of cortico-steroids is one of the promising managements available for plantar fasciitis. But it has significant debate about the associated complications. Plantar Iontophoresis with aqueous solution of Guggulu resin might be an effective alternative for the management of plantar fasciitis.



Iontophoresis being done with Aquous Solution of Guggulu

### REFERENCES

1. Singh D, Angel J, Bentley G, Trevino SG: Fortnightly review. Plantar fasciitis. *BMJ*. 1997; 315:172–5.
2. Rosenbaum AJ, DiPreta JA, Misener D, Plantar heel pain. *Med Clin North Am*. 2014 Mar;98(2):339-52. Epub 2013 Dec 10.
3. Peled E, Portal-Banker T, Norman D, Melamed E. Plantar fasciitis and extracorporeal shock wave therapy--essence, diagnosis and treatment methods Article in Hebrew. *Harefuah*. 2011 Feb;150(2):122-6, 206.
4. Lemont H, Ammirati KM, Usen N: Plantar fasciitis degenerative process (fasciosis) without inflammation. *J Am Podiatr Med Assoc*. 2003; 93:234–7.
5. Roxas M: Plantar fasciitis Diagnosis and therapeutic considerations. *Altern Med Rev*. 2005; 10:83–93.
6. Young CC, Rutherford DS, Neidfeldt MW Treatment of plantar fasciitis. *Am Fam Physician*. 2001; 63:467–74.
7. Goff JD, Crawford R. Diagnosis and treatment of plantar fasciitis. *Am Fam Physician*. 2011 Sep 15;84(6):676-82.
8. Li Z, Yu A, Qi B, Zhao Y, Wang W, Li P, Ding J. Corticosteroid versus placebo injection for plantar fasciitis: A meta-analysis of randomized controlled trials. *Exp Ther Med*. 2015 Jun;9(6):2263-2268. Epub 2015 Mar 24.
9. Lewis RD, Wright P, McCarthy LH. Orthotics Compared to Conventional Therapy and Other Non-Surgical Treatments for Plantar Fasciitis. *J Okla State Med Assoc*. 2015 Dec;108(12):596-598.
10. Satyavati GV: Gum Guggulu (Commiphora mukul) – the success story of an ancient insight leading to a modern discovery. *Indian J Med Res* 87: 327-335, 1988.
11. Setia RC, Parthasarthy MV and Shah JJ Development, histochemistry and ultrastructure of gum resin ducts in *Commiphora mukul*. *Engl. Ann Bot* 41: 999-1004, 1977.
12. Shishodia, S. and B.B. Aggarwal. Guggulu-sterone Inhibits nf-kappaB and kb kinase activation, suppresses expression of Anti-apoptotic gene products and enhances apoptosis. *J. Biol. Chem.*, 279: 47148-47158; 2004.

13. Kay, M.A. Healing with Plants in the American and Mexican West. The University of Arizona Press, Tuscon, pp: 221-224; 1996.
14. Kimura, IM. Yoshikawa, S. Kobayashi, Y. Sugihara and M. Suzuki New triterpenes, myrrhanol A and myrrhanone A, from *Gugguluugum resins* and their potent anti-inflammatory effect on adjuvant-induced air-pouch granuloma of mice. *Bioorg. Med. Chem.Lett.*, 11: 985-989; 2001.
15. Matsuda, H.T. Morikawa, S. Ando, H. Oominami, T. Murakami, I. Kimura and M. Yoshikawa : Absolute stereostructures of polypodane-type triterpenes, myrrhanol A and myrrhanone A, from Gugguluu-gum resin (the resin of *Balsamodendron mukul*). *Chem. Pharm. Bull.*, 52: 1200-1203; 2004.
16. De Leon, E.J., D.A. Olmedo, P.N. Solis, M.P. Gupta and M.C. Terencio : Diayangambin exerts immunosuppressive and anti-inflammatory effects *in vitro* and *in vivo*. *Plant Med.*, 68: 1128-1131; 2002.
17. Manjeet, K.R. and B. Ghosh: Quercetin inhibits LPS-induced nitric oxide and tumor necrosis factor-alpha production in murine macrophages. *Int. J. Immunopharmacol.*, 21: 435-443; 1999.
18. Santos, F.A. and V.S. Rao. Anti-inflammatory and antinociceptive effects of 1,8-cineole a terpenoid oxide present in many plant essential oils. *Phytother. Res.*, 14: 240-244; 2000
19. Gomez, M.A., M.T. Scienz, M.D. Garcia and M.A. Farnandez. Study on topical anti-inflammatory activity of *Achillea ageratum* on chronic and acute inflammation. *Z. Naturforsch. C*, 54: 937-941; 1999.
20. Duwiejua, M., I.J. Zeitlin, P.G. Waterman, J. Chapman, G.J. Mhango and G.J. Provan. Anti-inflammatory activity of resins from some species of the plant family Burseraceae. *PlantaMed.*, 59: 12-16; 1993.
21. Mohammad Ali Tahririan, Mehdi Motiffard, Mohammad Naghi Tahmasebi, and Babak Siavashi. Plantar fasciitis. *J Res Med Sci.* 2012 Aug; 17(8): 799–804. PMID: PMC3687890

**Cite this article as:**

Narinder Singh, Ashok Kumar, Alpona Ray, Alok Kumar. Plantar iontophoresis with aqueous solution of Guggulu in the management of Plantar fasciitis: Engendering an incipient dimension in its management. *J Biol Sci Opin* 2016;4(1):22-25 <http://dx.doi.org/10.7897/2321-6328.0416>

Source of support: Nil; Conflict of interest: None Declared

Disclaimer: JBSO is solely owned by Moksha Publishing House - A non-profit publishing house, dedicated to publish quality research, while every effort has been taken to verify the accuracy of the contents published in our Journal. JBSO cannot accept any responsibility or liability for the site content and articles published. The views expressed in articles by our contributing authors are not necessarily those of JBSO editor or editorial board members.