

**Review Report**

**SIMILE BETWEEN THE MODUS OPERANDI OF ANALGESIA OF TRAMADOL AND POISON OAK (RHUS TOXICODENDRON) ON FIBROMYALGIA**

**SUMAN BAGCHI\*1, SUMAN HALDER<sup>2</sup>, SHUBHAMOY GHOSH<sup>3</sup>, MOUSUMI ROY<sup>4</sup>**

<sup>1</sup>MD (Homoeopathy), SRF(H) at Dr. Anjali Chatterjee Regional Research Institute(H), Kolkata – 700035; Ex- Assistant Professor of Forensic Medicine & Toxicology, C.L.C. Homoeopathic Medical College, Hospital and Research Centre, Bilaspur (C.G.), <sup>2</sup>MD (Homoeopathy), SRF(H) at Dr. Anjali Chatterjee Regional Research Institute(H), Kolkata – 700035; Ex- Assistant Professor of Community Medicine, P.C.M. Homoeopathic Hospital and College, Kolkata., <sup>3</sup>MD (Homoeopathy), Head, department of Pathology & Microbiology, Mahesh Bhattacharyya Homoeopathic Medical College & Hospital (Govt. of W.B.), <sup>4</sup>BHMS, HMO at Chhurra, Raipur (Chattishgarh). Email: drsbagchi@gmail.com

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**ABSTRACT**

Fibromyalgia is a disorder characterized by widespread musculoskeletal pain accompanied by fatigue, sleep, memory and mood issues. Symptoms sometimes begin after a physical trauma, surgery, infection or significant psychological stress. In other cases, symptoms gradually accumulate over time with no single triggering event.

Women are much more likely to develop fibromyalgia than are men. Many people who have fibromyalgia also have tension headaches, temporomandibular joint (TMJ) disorders, irritable bowel syndrome, anxiety and depression.

Fibromyalgia is one of the most common chronic pain conditions. The disorder affects an estimated 10 million people in the U.S. and an estimated 3-6% of the world population. While it is most prevalent in women - 75-90 percent of the people who have fibromyalgia are women - it also occurs in men and children of all ethnic groups. The disorder is often seen in families, among siblings or mothers and their children. The diagnosis is usually made between the ages of 20 to 50 years, but the incidence rises with age so that by age 80, approximately 8% of adults meet the American College of Rheumatology classification of fibromyalgia.

While there is no cure for fibromyalgia, a variety of medications can help control symptoms. In general, treatments for fibromyalgia include both medication and self-care. The emphasis is on minimizing symptoms and improving general health. Medications can help reduce the pain of fibromyalgia and improve sleep. Common choices include: **Analgesics (Tramadol)**. In this article we like to discuss on the similarity of action between the analgesic medicine (Tramadol) and the homoeopathic medicine Poison oak (Rhus toxicodendron) on fibromyalgia from the aetiopathogenetic point of view. Poison oak, a wild growing plant of the anacardiacea family is widely distributed and easily accessible and also a very common Homoeopathic remedy as Rhus toxicodendron.

**Keywords:** Analgesic medicine, drug toxicity, Fibromyalgia, Pharmacological actions, Rhus toxicodendron.

**INTRODUCTION**

Fibromyalgia (FM) is a syndrome characterized by medically unexplained, widespread musculoskeletal pain, hyperalgesia and/or allodynia, physical and mental fatigue and effort intolerance, non-restorative sleep, mood disturbance as well as other functional (e.g. gastrointestinal) complaints. [1]

Although the exact aetio-pathogenesis of FM is not known, the precipitating and predisposing role of physical and psychosocial stress are responsible in the development of FM. Several retrospective case-control studies have shown that traumatic experiences (neglect, maltreatment or abuse) during childhood are more frequently reported by FM patients than by medically ill or healthy controls. [2].

**Stress and Fibromyalgia**

A current paradigm to explain the complexity of FM symptomatology proposes that it is a “stress related syndrome” in which a disordered hypothalamic-pituitary-adrenal (HPA) axis acts as a final common pathway linking FM to other “stress-related” somatic and psychiatric syndromes. [3]

Stress causes Sleep disorders. FM is seen in particularly those patients have an abnormal sleep pattern involving stages 3 and 4 of non REM sleep [4]. The Growth Hormone (GH) is secreted predominantly during stages 3 and 4 of non-REM sleep. There are close links between the Hypothalamo-Pituitary Axis (HPA) and the HP-growth hormone (GH) axis. The Growth hormone is the only

pituitary hormone that is under the influence of both stimulatory and inhibitory hypothalamic hormones. The normal pulsatile secretion of GH depends on the tonic balance of stimulatory growth hormone releasing hormone (GHRH) and inhibitory somatostatin (SRIF). [5] Under normal circumstances the production of GH occurs only when the secretion of GHRH takes place in the setting of low levels of somatostatin tone. [6] Thus the regulation of GH secretion is dependent on the relative amounts of GHRH and somatostatin that are released from the hypothalamus into the hypothalamic-hypophyseal portal venous system.

Now under the stress there is dysregulation of HPA axis, as a result deficiency of GHRH and finally deficiency of secretion of GH.

On the other hand, many biological “stresses” such as severe exercise, trauma and haemorrhage lead to an increase in plasma glucocorticoid concentration resulting from release of CRH (Corticotrophin-releasing hormone) from the hypothalamus. This natural hormone (CRH) is only one of a number of natural and synthetic *corticotrophin-releasing factors* (CRF) which can promote the release of ACTH (Adreno-corticotrophic hormone) from the anterior pituitary [7]

Neck has hypothesized that a stress induced increase in CRF is the common denominator linking the disturbed HPA axis and reduced GH secretion in FM [8].

There is a critical link between the increases CRF and hypothalamic somatostatin tone [9]. Increase somatostatin (other name is *growth*

*hormone-release inhibiting hormone*) inhibits the GHRH and also reduces GH secretion.

Growth hormone deficiency in adults has been associated with a miscellany of symptoms that are similar to those described by FM patients: low energy, poor general health, reduced exercise capacity, muscle weakness, cold intolerance, impaired cognition, and decreased body mass. GH is important in maintaining muscle homeostasis, and it was theorized that sub-optimal levels might be a factor in the impaired resolution of muscle micro-trauma in FM patients. [10]

#### Role of Glucocorticoids in the development of fibromyalgia:

Glucocorticoids (mainly cortisol) accelerate gluconeogenesis in the liver, mainly by favouring glycogen formation from amino acids formed by protein breakdown. The protein in question may come partly from peripheral tissues e.g. muscle. As a result wasting of the muscle the patient feels pain. [7]

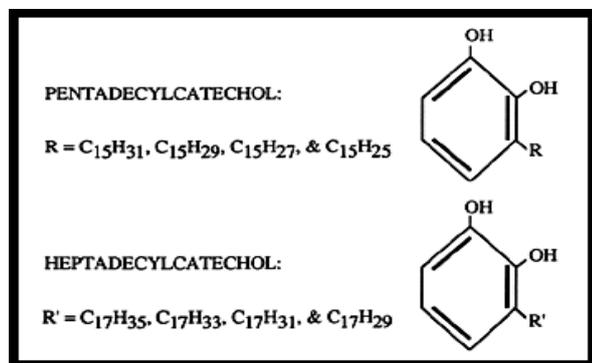
#### Most common medicine used in modern medicine for Fibromyalgia:

ULTRAM® or Tramadol hydrochloride. [11]

#### Pharmacology of Ultram (tramadol hydrochloride):

ULTRAM® (Tramadol hydrochloride) contains tramadol, a centrally acting synthetic opioid analgesic. Although its mode of action is not completely understood, from animal tests, at least two complementary mechanisms appear applicable: binding of parent and M1 metabolite to  $\mu$ -opioid receptors and weak inhibition of reuptake of norepinephrine and Serotonin. (The catecholamine norepinephrine is a neuro-modulator of the peripheral sympathetic nervous system but is also present in the blood mostly through "spill over" from the synapses of the sympathetic system). [12]

So, the main action of the ULTRAM® is inhibition of norepinephrine and serotonin which are responsible for production of pain in FM.



**Fig. 1.** Chemical structure of urushiols found in resin canals of poison oak and poison ivy. Poison ivy mostly contains a mixture of four pentadecylcatechols (with 15-carbon side chain), while poison oak contains a mixture of four heptadecylcatechols (with 17-carbon side chain). Now raw Poison oak juice can produce the symptoms like of FM (Pain, joint stiffness etc.) because presence of the catechols.

#### The action of Poison oak on Fibromyalgia

Freshly cut stem of *Rhus toxicodendron* (RT) showing adventitious roots and black lacquer oozing from resin canals in the inner bark. The resinous sap is produced in resin canals of the stems, roots, leaves and flowers. J.H. Langenheim (2003) discusses resins of the sumac family (*Anacardiaceae*) in her book entitled *Plant Resins: Chemistry, Evolution, Ecology, and Ethno botany*. Cross sections of RT stems show distinct concentric annual rings (ring-porous wood). Numerous resin canals appear as tiny black dots and are confined to the phloem layer just inside the bark which principally contains urushiol responsible for giving poison oak its bad reputation due to its involvement in promoting allergic reaction. The name is derived

from "urushi," Japanese name for lacquer made from the sap of the Japanese lacquer tree ("kiurushi" or "urushi ki"). [13] Urushiol is a transparent, non volatile olioresin which turns into a brownish lacquer when oxidized. It is basically a mixture of phenolic compounds called catechols. [14] [A catecholamine (CA) is a monoamine, an organic compound that has a catechol (benzene with two hydroxyl side groups) and a side chain amine][15], potent benzene ring compounds with a long side-chain of 15 or 17 carbon atoms (Figure 1). According to Dawson-The side chain may be saturated or unsaturated with one, two, or three double bonds. The remarkable immune reaction and specificity of the catechol molecule is determined by the long side-chain. [16] Poison oak urushiol contains mostly catechols with 17 carbon side-chains (heptadecylcatechols), while poison ivy and poison sumac contain mostly 15 carbon side-chains (pentadecylcatechols). See Figure 1 below

Now in the homeopathic preparation of RT it is serially diluted and potentized and then its symptom producing capability is assessed through a procedure known as 'proving'. Homeopathy stands on the law "**Similia Similibus Curantur**". It means which can produce the disease in crude form the same can cure the same disease in its potentized form (This law was established by Hahnemann in 1796, after proving of Chinchonabark on himself which produced malaria like symptoms in crude form. [17] For this reason when RT is applied on the patient of FM then it relieves the pain because then it blocks the action of catecholamines.

"Double blind trials have been conducted using the homeopathic remedy *Rhus Tox*, and according to a report submitted by the Complimentary and Alternative (CAM) Review Board in September 2009, results are promising. Reports indicate that fibromyalgia patients taking the remedy have experienced a significant reduction in pain, stiffness and weakness from fibromyalgia pain. *Rhus Tox* is well known for the treatment of musculoskeletal conditions. *Rhus Tox* is available at health food stores and may be administered at home, but patients should see a qualified homeopath for suggestions concerning frequency and dosage." [18]

"*Rhus tox* also induces pains, apparently of a rheumatic kind and which are felt not only in the limbs but in the body though most especially about the joints. The structures most powerfully affected appear to be the fibrous ones. The pains in questions are accompanied by a very slight amount of swelling, singular to say, they become intensified by rest and warmth. Sleep is greatly disturbed, and the patient becoming restless, constantly turning about and often suffering from great nervous depression." [19]

#### CONCLUSION

Fibromyalgia remains a challenging condition. However, clinical studies have demonstrated that fibromyalgia patients can reduce their symptoms through a variety of treatment options. After the above discussion it is clear that analgesic medicine Ultram® and the homeopathic medicine *Rhus toxicodendron* act on the same plane i.e. blocking the pain modulator catecholamines and thereby establishing is a similarity in their modus operandi.

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