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Mohammad Zakir Siddiqui
Ph. D Scholar Unani Medicine
Faculty of Natural Sciences,
Jamia Millia Islamia, New Delhi,
India

Sada Akhtar
MD Scholar Unani Medicine
Department of Ilmul Advia,
AKTC, AMU, Aligarh, India

Correspondence
Mohammad Zakir Siddiqui
Ph. D. Scholar Unani Medicine
Faculty of Natural Sciences,
Jamia Millia Islamia, New Delhi,
India

Suranjan shirin (*Colchicum autumnale*): A review of an anti-arthritic Unani drug

Mohammad Zakir Siddiqui and Sada Akhtar

Abstract
Arthritis is one of the most prevalent disease and among the biggest health care problems which affects hundreds of millions of people throughout the world and is a leading cause of disability in the community. Tibb-e-Unani claims to possess a number of effective and safe drugs useful in the treatment of arthritis. Suranjan Shirin (*Colchicum autumnale*) is an important drug of Unani Medicine commonly used in the management of Waja ul Mafasil (Arthritis). It is mentioned by all renowned Unani authors in their books as a primordial drug in arthritis. Suranjan Shirin is a perennial herb belongs to the family Colchicaceae. The corms of *Colchicum autumnale* is chiefly used to relieve the pain and inflammation and shorten the duration of acute gout and certain gouty infections. It is also used for external application to lessen inflammation and pain. The present paper also reviews recent investigations carried out on Suranjan Shirin during recent times.

Keywords: Arthritis, waja ul mafasil, Suranjan shirin, *Colchicum autumnale*.

Introduction
Suranjan Shirin is also known as "Autumn crocus" or "Meadow Saffron" belongs to family Colchicaceae (previously Liliaceae) (Toplan *et al.*, 2016) [1]. Suranjan believed to have been derived from species of Colchicum have long been known under the names of "colchicum", "hermodactyl'', "surinjan" and "ephemeron'' and some have been identified as *Colchicum autumnale*. Colchicum extracts were first described as a treatment for gout in De Materia Medica by Dioscorides in the 1st century AD (Trease & Evans, 2009) [2]. Its name comes from Colchis or Colchis, an ancient Georgian state and Kingdom on the eastern shore of the black sea, where plants were widespread (Imazio *et al*., 2009) [3]. Suranjan-al-Halu, Qalb-al-Arz, Balbusa, Aqeemaroon, Falchion, Burberry and Jangli Singhara are some of its vernacular name (Baitar, 1999) [4]. It is perennial herb up to 30 cm tall which is commercially grown in Italy and Yugoslavia (Bhattacharjee, 2004) [5]. Colchicum corm is the contracted subterranean stem of the meadow saffron, *Colchicum autumnale* (Anonymous, 1999). It is widely distributed in Europe, the Mediterranean region, Central Asia and Northern India (Anonymous, 2001) [7]. Early Arabian writers including renowned Unani physician and Author "Abu Sahl 'Isa ibn Yahya al-Masihi" (d. 1010 CE / 401 AH) described three kinds of Hermodactyl or Suranjan i.e. White, Yellow and Black. Mir Muhammad Hussain in his book *Makhzan* described that white variety is best which is not bitter in taste, next to it is yellow variety which can be used internally like white variety while the black variety is poisonous which can be only used externally. Habish Bin-ul-Hasan also states that white variety is the best while yellow and black variety is toxic (Baitar, 1999) [4]. There are two varieties commonly sold in Indian market; one is sweet and the other bitter. The bitter variety *Colchicum luteum* or Suranjan Talkh is distinguished from the sweet variety Suranjan Shirin by its bitter taste, smaller size, darker colour and a reticulated appearance of the corms. Attempts have frequently been made to introduce *C. autumnale* into India but with very little success. Though the *C. autumnale* does not grow in India, a very good substitute in the form of *C. luteum* Baker is available (Chopra *et al*., 1958) [8]. The drug was recommended in Arabian writings for use in gout but it was little employed in either classical or medieval times owing to the wholesome fear inspired by its poisonous nature. Colchicum corm appeared in London Pharmacopoeias of 1618, 1627, 1632, 1639. It was then deleted but reappeared in the edition of 1788. The uncertain action of the corm led Dr. W. H. Williams, of Ipswich, to introduce the use of the seeds in 1820 (Trease & Evans, 2009) [2]. The corms and seeds of *Colchicum autumnale* are official in the British Pharmacopoeia and are used extensively in western medicine as a sovereign remedy for gout (Chopra *et al*., 1958) [8]. John Lindley in his book

Flora Medica described that the best time for collection of the corm of *Colchicum autumnale* is just after withering of leaves and should be used without loss of time (Lindley, 1981) [9]. According to Najmul Ghani, corm of colchicum is mainly used for medicinal purpose and the efficacy of the drug remains for three years (Ghani, 2010) [10]. It is chiefly used to relieve the pain and inflammation and shorten the duration of acute gout and certain gouty infections, but is liable to cause intestinal pain accompanied by vomiting and purging (Anonymous, 1999). Dried Colchicum corm contains up to about 0.6% of the alkaloid Colchicine (Wallis, 1985) [11]. Colchicine was isolated by Pelletier and Caventouin 1820 (Trease & Evans, 2009) [2]. On treating with sulphuric acid (70%) or concentrated HCL produces yellow colour due to colchicine (Ali, 2012) [12].

Botanical description

Macroscopically, fresh corm appears 2-3 cm in diameter, but the dried corm consists of somewhat reniform, transverse slices and occasional more ovate longitudinal slices, about 2-5 mm thick. The epidermal surface is cinnamon-brown and slightly wrinkled. The interior is white and starchy and, if carefully smoothed, shows scattered fibrovascular bundles. The drug breaks with a short mealy fracture. The odour is much less marked than in the fresh drug. The taste of corm is either slightly lesser bitter then *C. luteum*, sweet or tasteless. Microscopically, it shows numerous starch grains contained in parenchyma, some simple but the majority consisting of two to seven components. Individual grains are from 6 to 30 µm diameter, and show triangular or star shaped hilum. Their shape varies from spherical or ovoid to polygonal. Vessels with a spiral or annular thickening and portions of brownish epidermis with very occasional circular stomata may also be seen (Trease & Evans, 2009) [2].

Cultivation and collection

The corm consists of an enlarged underground stem bearing foliage leaves sheathing leaves and fibrous roots. In the later part of the summer, a new corm develop in the axil of a scale leaf near the base of the old corm, the new plant occupying an in folding in the side of the parent corm. In September the parent corm bears the remains of recently withered leaves and is very much larger than the daughter corm. For medicinal purposes the corm would have been collected shortly after the withering of the leaves that is at early summer and before the enlargement of its axial bud. The young corm develops fibrous root at its base and in August or September two to six flowers emerges from it, but its foliage leaves do not appear above ground until the following spring. The corm are collected in July, cut into transverse slice and dried at a temperature not exceeding 65 ℃ (Trease & Evans, 2009) [2].

Preservation and Storage

Drug should be kept in air tight containers at cool and dry places (Wallis, 1985) [11].

Mizaj (Temperament)

With the consensus of various Unani authors the temperament of Suranjan is hot 3^0 and dry 2^0 along with slight variation in grade of temperament (Azam 2014; Ghani, 2010; Anonymous, 2010) [13, 10, 14].

Actions

Its chiefly possesses antiinflammatory, analgesic and antiarthritic activity. It also possess expectorant, deobstruent, antidote and aphrodisiac activity (Ghani, 2010; Kabeeruddin 2007; Hakeem 2002) [10, 15, 16].

Therapeutic activity

It is chiefly used to relieve the pain and inflammation and shorten the duration of acute gout and certain gouty infections (Wallis, 1985) [11]. It is also prescribed to treat myeloid leukemia (Ali, 2012) [12]. It increases the secretions of skin, liver and kidneys and also the flow of bile. In ascites due to liver disease it is a very efficacious remedy. In cerebral and hepatic congestions it acts as a purgative with benefit. It is also found efficacious in genital infections like gonorrhea (Khory & Katrak, 1993) [17]. The extracted colchicine is employed orally in tablet form for arthritis, familial Mediterranean fever while corm and seeds are used to treat enlarged prostate, dropsy and gout, rheumatism and arthritis (Bhattacharjee, 2004) [5]. It is also used to treat sciatica and to increase Aphrodisiac activity (Ghani, 2010; Kabeeruddin, 2007) [10, 15].

Muzir (Adverse Effects)

It has adverse effects on stomach (Azam 2014; Sina, 2014) [13, 18] and liver (Ghani, 2010; Kabeeruddin, 2007) [10, 15].

Musleh (Correctives)

The musleh or correctives of Suranjan Shirin (*Colchicum autumnale*) are Kateera *(Sterculia urens*), Zaafraan (*Crocus sativus)*, Sugar (Ghani, 2010; Kabeeruddin, 2007) [10, 15], Zanjabeel *(Zingiber officinale)*, Filfil-e-Siyah *(Piper nigrum)* and Murabba Amla (Hakeem, 2002) [16].

Badal (Substitute)

The various substitutes (abdal) of Suranjan Shirin (*Colchicum autumnale*) mentions in various Unani literatures are Heena *(Lawsonia inermis*), Muqil (*Commiphora mukul)* in half dose as of Suranjan (Sina, 2014) [18], Suranjan Talkh (*Colchicum luteum*), Aftimun (In one third dose of Suranjan) and Kharbaq-Safed (*Veratrum album*) in one tenth dose of Suranjan (Ghani, 2010) [10].

Miqdar-e-Khurak (Dosage)

The various dosage of Suranjan Shirin (*Colchicum autumnale*) mentions in various Unani classical literatures are 2-6 gram as single drug, 2.25 – 6.25 gram (In compound formulations) and 10.5 – 17.5 gram as decoction (Ghani, 2010; Hakeem, 2002) [10, 16].

Unani Murakkabat (Formulations)

The important Unani formulations of Suranjan Shirin (*Colchicum autumnale*) are Raughan-e-Waja ul Mafasil, Habb-e-Suranjan and Majoon-e- Suranjan (Kabeeruddin, 2007; Safiuddin, 1993) [15, 19].

Phytochemical studies

Dried colchicum corm contains up to 0.6% of the chief alkaloid Colchicine and abundance of starch. It yields 2.2 to 2.4% of ash (Wallis, 1985) [11]. Colchicine is an amorphous, yellow white alkaloid readily soluble in water, alcohol or chloroform. It also contains alkaloids like colchicine, colchicine, demecolcine, etc. (Ali, 2012) [12]. Colchico-resin, β-colchicoresin, a trace of veratrine, fat, gum, sugar, tannin and gallic acid is also present in colchicum (Khory & Katrak, 1993) [17]. Lecanu analyzed the tasteless variety and found

that the corm contains starch (forming the bulk of the drug), fatty matter, gum, supermalates of lime and potash and chloride of potassium (Dymock, 1891) [20]. Phytochemical analysis of hydroalcoholic extract of *Colchicum autumnale* flower and root showed the presence of flavonoids, Tannins, terpenoids, polyphenols while carbohydrate and protein were absent (Bunghez *et al*., 2017) [21]. Ellington *et al*., (2003) [23] reported the extraction of alkaloids colchicine, 3- dimethyl colchicine and colchicoside from seeds of *Colchicum autumnale* by supercritical carbon dioxide method. The quantitative determination of the alkaloids was performed by HPLC and the percentage of recovery was higher than 98% for the three alkaloids. This extraction procedure was compared with a conventional method involving maceration and sonication, and the same levels of alkaloids were obtained in each case. The supercritical carbon dioxide method is, however, very efficient, more rapid and more environmental friendly than conventional methods. Another study reported the presence of 6 chemical constituents in the flowers of *Colchicum autumnale* which was introduced from Europe to China i.e. colchicine, 2- demethyl colchicine, 2- demethyl colchicine 2- demethyl β- lumicolchicine, 2- demethyl demecolcine and β- lumicolchicine. It is also reported in the study that the content of colchicine was low while the content of 2- demethyl colchicine was high in the flowers of *Colchicum autumnale* (Ping *et al*., 1999) [22].

Pharmacological studies

Suranjan Shirin (*Colchicum autumnale*) was found effective in all the three important of arthritis i.e. rheumatoid arthritis, osteoarthritis and gouty arthritis. It comprise good anti-inflammatory and anti-arthritic activity in all three major types of arthritis which is equivalent to the effect of the potent standard inflammatory agent Diclofenac sodium (Viquar *et al*., 2012) [26]. It was clinically evaluated that *Colchicum autumnale* is effective in the treatment of gouty arthritis as an ingredient of Gouticin tablet (Akram, 2010) [27] and in the treatment of rheumatoid arthritis as an ingredient of Arthritin tablet (Asif, 2012) [28]. An agglutinin isolated from *Colchicum autumnale* tuber, *Colchicum autumnale* agglutinin (CAA) activates all murine T-lymphocyte but does not induce the proliferation of all activated cells. It induces the proliferation of a fraction of the CD4+ and CD8+ mouse T-lymphocytes. All T-lymphocytes are activated and express high levels of the activation markers CD69 and CD44 (Bemer *et al*., 1996) [24]. Acute poisoning of *Colchicum autumnale* was reported in cattle through experimental histopathological study. Crude or dehydrated bulbs of autumn crocus (*Colchicum autumnale* L.) were fed to eleven calves. All the calves developed severe diarrhoea and died or euthanized within 63 hr. At necropsy, the gastro-intestinal mucosa was oedematous and hemorrhagic. Histologically, necrosis and degeneration with karyopyknosis and karyorrhexis were shown in the basal cell layer of the tongue, esophagus, forestomach, renal pelvis, urinary bladder, neck cell layer of the abdominal gastric glands, and intestinal crypts. These findings were also seen in Kupffer cells, renal tubular epithelial cells and lymphocytes in the lymphoid and hemopoietic systems. The lesion of the present acute crocus poisoning of cattle closely resembled those reported in humans with colchicine intoxication. Refined acetone extract of organs of poisoned cattle proved to contain colchicine and demecolcine by high performance liquid chromatography (Yamada *et al*., 1998) [25]. Another study reported suicidal plant poisoning with *Colchicum autumnale.* It is commonly known as autumn crocus, and as 'gowri gedde' in the southern region of Karnataka State in South India. A twenty four year old man consumed 'gowri gedde' to end his life. Initially he presented with severe vomiting, diarrhoea and epigastric pain. He died on the third day of ingestion due to multiorgan failure. Chemical analysis of blood and viscera obtained post-mortem confirmed the presence of colchicine. Colchicine poisoning is potentially life threatening because of its high toxicity and unavailability of specific antidote treatment. It classically presents with gastroenterocolitis and may result in multiorgan failure in fatal cases (Nagesh *et al*., 2011) [29]. In an observational study, *Colchicum autumnale* (CAU) positively changed the clinical pathology of subclinical hyperthyroidism and thyroidal volume in patients with euthyroid goitre by normalization of the regulation of thyroidal hormones. Linear regression for TSH and fT3 indicated a regulative therapeutic effect of *Colchicum autumnale* (Scheffer *et al*., 2013) [30].

Conclusions

Arthritis is one of the leading causes of physical impairment and disability in the community which affects hundreds of millions of people throughout the world. Although Western medicine possesses many anti-inflammatory and anti-arthritic drugs but they are neither optimally effective nor safe. So, Traditional Medicines, including Tibb-e-Unani are being explored for effective and safe anti-arthritic drugs. It was concluded from the literature review that Suranjan Shirin (*Colchicum autumnale*) is mentioned in Unani classical literature for its various therapeutic efficacies but specifically in arthritis. Several preliminary studies reported its effectiveness in different forms of arthritis. Therefore, *Colchicum autumnale* must be further explored for high throughput screening, scientific validation and comparative effectiveness in different forms of arthritis like osteoarthritis, rheumatoid arthritis, gouty arthritis etc. Its active constituents must be isolated and their pharmacological activity must be screened. The two Indian species of Colchicum i.e. Suranjan Talkh and Suranjan Shirin also compared for its potency and efficacy with safety. Since, various studies reported its poisoning in humans as well as in cattle, therefore, its dose must be established which will be optimally effective and safe. Before evaluating its pharmacological activity it should also be standardized to ensure uniformity in therapeutic efficacy.

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