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REVIEW

Safety and Efficacy of Shilajit (Mumie, Moomiyo)

Sidney J. Stohs*
School of Pharmacy and Health Professions, Creighton University Medical Center, Omaha, NE 68168, USA

Shilajit (mumie; moomiyo, mummiyo) has been used for a wide variety of illnesses and conditions for many years. However, relatively few well-controlled human studies have been conducted on the effects of shiliajit, although a growing number of studies have been published in recent years involving animal and *in vitro* systems. The safety of shilajit is well documented based on animal and human studies. Various research studies indicate that shilajit exhibits antioxidant, anti-inflammatory, adaptogenic, immunomodulatory, and anti-dyslipidemic properties. Animal and human studies indicate that shilajit enhances spermatogenesis. Furthermore, animal and human data support its use as a 'revitalizer', enhancing physical performance and relieving fatigue with enhanced production of ATP. Key constituents in shilajit responsible for these effects appear to be dibenzo-α-pyrones and fulvic acid and their derivatives. Various mechanistic studies provide support for the above observed effects. Additional well-controlled human and animal studies involving the use of standardized products are needed. Copyright © 2013 John Wiley & Sons, Ltd.

Keywords: shilajit; mumie; moomiyo; mummiyo; safety; efficacy; active ingredients; mechanisms.

INTRODUCTION

Shilajit is a herbo-mineral exudate with a long history of use in traditional folk medicine. This material is called mumie, moomiyo, or mummiyo as well as various other lesser used names. It is derived from mountainous regions of India (Goshal, 2006; Wilson *et al.*, 2011), Russia, the former USSR (Ural, Altai, Caucasus, Kazakhstan, Sayan, Baykal, Uzbekistan, and Tajikistan), and other countries as China, Pakistan, Nepal, Afghanistan, and Tibet (Schepetkin *et al.*, 2002).

Shilajit is used in folk medicine to treat bone fractures, stomach disorders, inflammation of joints, impotence, nervous and cardiovascular issues, and strains of muscles and tendons. It is also purported to be an effective treatment for stomach ulcers, wounds, diabetes, and urinary tract infections. Numerous anecdotal reports of therapeutic uses exist, while very few well-designed, placebo-controlled human and animal studies which have undergone peer review have been published.

Based on published research studies, it is believed to be an antioxidant, anti-inflammatory, chemoprotectant, and immunomodulator and exhibit adaptogenic and potent anabolic properties (Acharya *et al.*, 1988; Schepetkin *et al.*, 2002; Ghosal, 2006; Agarwal *et al.*, 2007; Wilson *et al.*, 2011). In the former USSR, it was used secretly for many years to enhance performance (physical and mental) of Olympic athletes and special military forces, reduce stress-related injuries, and benefit recovery (Bucci, 2000; personal communication with Dr. N. Volkov).

* Correspondence to: School of Pharmacy and Health Professions, Creighton University Medical Center, Omaha, NE 68168, USA, 7068 Maumee Valley Court, Frisco, TX 75034, USA
E-mail: sstohs@yahoo.com

CHEMISTRY

Shilajit is a brown to black herbo-mineral resinous exudate that is extruded during the hottest months of the year from layers of rocks in various mountainous regions noted above. The exudates may collect on rock surfaces or be imbedded in rock sediments. The composition of shilajit will depend upon various geographic and environmental factors including minerals present, indigenous plants, humidity, temperature, molds, and bacteria that may be involved, and atmospheric and geothermal pressures (Ghosal 2006; Agarwal *et al.*, 2007).

The chemical composition of shilajit also depends upon whether it is raw material or processed in some manner. A pulverized but unprocessed material may contain 60–80% organic matter and 20–40% mineral content (Goshal *et al.*, 1991; Frolova and Kiseleva, 1996; Schepetkin *et al.*, 2003). For example, an unprocessed material may contain organic acids as fulvic acids, protein, gums, amino acids, humic acid, hippuric acid, waxes, steroids, essential fatty acids, vitamins, and up to 30% inorganic constituents consisting primarily of calcium, potassium, and magnesium (Frolova and Kiseleva, 1996; Ghosal, 2006; Agarwal *et al.*, 2007).

'Purified' shilajit products possess variable consistency depending on the manner in which they are processed and their geographic origin (Schepetkin *et al.*, 2003; Ghosal, 2006; Raju, 2012). The most common method of purification involves exhaustive water extraction with the removal of insoluble impurities by filtration. The filtrate is concentrated by removing the water with heat or sunlight. In some cases, neutral aqueous salt solutions and citrate buffer are used to perform the initial extraction (Ghosal, 2006). A typical processed product may contain 50–60% fulvic acid and equivalents (polymers and related structures), 0.3–0.4% dibenzo-α-pyrones (DBPs), 10–30% DBP chromoproteins (DCPs), and 10–15% minerals. Products are frequently standardized

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using DBPs, DCPs, and fulvic acids, with fulvic acid and equivalents being the most common standard (Raju, 2012).

With respect to minerals in processed shilajit, the sum of potassium, calcium, and magnesium generally makes up over 90% of the total mineral content, with sulfur and sodium being the next most common minerals (Raju, 2012). However, as many as 40 or more total minerals have been reported (Frolova and Kiseleva, 1996), with the majority of these in small or trace amounts. Color variations of shilajit are primarily due to differences in mineral content such as the amounts of iron, copper, and silver (Ghosal 2006; Agarwal *et al.*, 2007).

Because of the complex nature of this material, the difficulty in providing standardized material, and the relative rarity of the material, adulterated and counterfeit products are marketed as shilajit (moomiyo, mumie) (Schepetkin *et al.*, 2003).

ACTIVE CONSTITUENTS

The physiological and pharmacological effects of shilajit are attributed to the DBPs, DBP chromoproteins (DBPs conjugated to proteins), fulvic acid, and various polymeric forms of fulvic acid (Ghosal, 2006; Sharma *et al.*, 2003; Schepetkin *et al.*, 2003; Raju, 2012). Several studies involving these constituents are described below. Some individuals in early studies believed that the primary effects of shilajit were due to the ability of fulvic acid constituents to chelate the minerals associated with the product and facilitate cellular penetration (Agarwal *et al.*, 2007; Carrasco-Gallardo *et al.*, 2012).

The overall mineral content of shilajit is small with the primary minerals being potassium, calcium, and magnesium. At the doses given, it is doubtful that significant amounts of minerals are absorbed and penetrate cells since the vast majority of minerals that are present occur in exceedingly small amounts. For example, in a typical shilajit dose of 200 mg, the total mineral content will be 2–3 mg, with about 90% being potassium, calcium, and magnesium. To put this in perspective, the typical daily recommended intake for calcium is 1000–1200 mg, while the daily values for magnesium and potassium are 400 mg and 3000 mg, respectively.

RESEARCH STUDIES

In spite of the fact that shilajit (moomiyo, mummiyo, and mumie) has been used in folk medicine in India and Northern Asia for thousands of years (Schepetkin *et al.*, 2002; Agarwal *et al.*, 2007; Wilson *et al.*, 2011), and in performance enhancement in the former USSR for many years, few published, peer-reviewed scholarly publications exist in the scientific literature involving human subjects. Much of the early literature involves anecdotal reports, poorly controlled studies with products of unknown composition, and publication in obscure journals (Schepetkin *et al.*, 2002; Goshal, 2006; Agarwal *et al.*, 2007; Wilson *et al.*, 2011). Furthermore, in the former USSR, most research regarding moomiyo (mumie, shilajit) has been classified and has not been published.

A growing number of studies in animals and *in vitro* systems using standardized materials are being published, and the chemical composition of shilajit has been examined by various investigators. The following summarizes available published research studies as well as a number of unpublished research reports involving well-designed studies.

Safety studies

Various studies have assessed the safety of shilajit. The acute LD50 of a purified shilajit in rats was reported to be 1000 mg/kg when given intraperitoneally (IP) and greater than 2000 mg/kg when given orally (Acharya *et al.*, 1988). In rabbits and mice given 100 mg/kg and 500 mg/kg mumie (shilajit) orally in water for 30 days, no morphological or histological changes in internal organs were observed (Kelginbaev *et al.*, 1973).

In a subchronic toxicity study (Anisimov and Shakirzyanova, 1982), mumie (shilajit) was given to rats at doses of 200 mg/kg and 1000 mg/kg for 90 days and produced no adverse effects on heart, liver, kidneys, blood cells, or nervous and endocrine systems. Furthermore, mumie (shilajit) did not elicit any embryotoxic or teratogenic effects in pregnant rats (Anisimov and Shakirzyanova, 1982) or mice (Al-Hamaidi *et al.*, 2003). Ghosal (2006) reported that the LD50 of fulvic acids isolated from shilajit in rats was 1268 mg/kg when given orally, indicating a low order of toxicity.

In an unpublished acute toxicity study, 'purified' (processed and standardized) shilajit (PrimaVie®) administered to rats at an oral dose of 2000 mg/kg was well tolerated, and at doses of 200 mg/kg and 400 mg/kg orally for 90 days did not produce any hepatic, renal, hemopoietic, or behavioral effects (Raju, 2012). Furthermore, no significant changes in weights of vital organs were observed as compared to control animals. In a mouse study, doses of 10 mg/kg, 30 mg/kg, and 100 mg/kg of processed shilajit (PrimaVie®) did not produce any metaphase chromosomal aberrations in bone marrow (Raju, 2012), indicating that it was not genotoxic.

In a placebo-controlled study, 20 healthy subjects were given 2000 mg processed shilajit daily for 45 days in capsule form (Sharma *et al.*, 2003). No significant changes in heart rate, blood pressure, or body weight were observed. Furthermore, shilajit had no effect on the following blood chemistry parameters: glucose, urea, creatinine, uric acid, total protein, albumin, albumin/globulin ratio, alkaline phosphatase, ALT (alanine amino transferase, SGPT), or AST (aspartate amino transferase, SGOT). The results indicated no evidence of systemic toxicity by shilajit under these experimental conditions.

The administration of processed shilajit (PrimaVie®) at a dose of 100 mg twice a day to 28 male subjects for 90 days had no significant effect on renal profile parameters including urea, albumin, total protein, globulin, uric acid, bilirubin, alkaline phosphatase, ALT (SGPT), or AST (SGOT) (Biswas *et al.*, 2009). Small but significant decreases in fasting blood glucose and creatinine levels were observed in shilajit-treated subjects. The results indicate

that under these conditions, shilajit produced no evidence of systemic toxicity.

In an unpublished safety study in human volunteers (Raju, 2012), processed shilajit (PrimaVie®) was given to healthy subjects at a dose of 250 mg twice a day for 90 days. No changes in hepatic or renal functions, vital signs, or blood parameters were observed, and no adverse effects were reported.

In summary, in both animal and human studies, shilajit (mumie) has demonstrated a high degree of safety.

Human efficacy studies

Several human efficacy studies have been published. In a double-blind, placebo-controlled study, Sharma *et al.* (2003) administered 2000 mg of processed shilajit or placebo per day for 45 days. Twenty subjects received the shilajit, while 10 subjects received the placebo. Significant decreases in serum cholesterol, LDL, VLDL, and triglycerides were observed in response to shilajit relative to the placebo group. Improved antioxidant status was noted in the form of increases in superoxide dismutase, vitamin C and vitamin E. HDL also increased in response to shilajit.

A clinical study evaluating the spermatogenic activity of shilajit was conducted by Biswas *et al.* (2009). Thirty-five infertile (oligospermic) male subjects were enrolled in the study and given 100 mg processed shilajit (PrimaVie®) in capsule form twice a day for 90 days. The 28 subjects who completed the study showed significant increases in normal (18.9%) and total (61.4%) sperm count and sperm motility (12.4–17.4%). A significant decrease in semen malondialdehyde levels indicated that shilajit exhibited antioxidant activity. Furthermore, shilajit treatment resulted in significant increases in serum testosterone (23.5%) and FSH (9.4%) levels, results which supported the increase in sperm count.

In an unpublished pilot study involving six healthy human volunteers, 200 mg processed shilajit (Primavie®) was given once daily for 15 days. Treatment with shilajit significantly increased energy production and physical exercise (Harvard step test) (Raju, 2012). The increase in energy production was confirmed based on increases in ATP, ATP/ADP ratio, coenzyme Q10 (CoQ10), total adenine nucleotides, adenylate energy charge, and uric acid levels in whole blood. This study suffers from the lack of an adequate number of subjects.

Animal and *in vitro* studies

One of the earliest well-designed series of studies on the pharmacological effects of shilajit was performed in various animals species (Acharya *et al.*, 1988). Shilajit at a dose of 200 mg/kg IP was shown to exhibit significant analgesic activity relative to control based on the rat tail flick method. Shilajit at a dose of 50 mg/kg IP decreased carrageenan-induced inflammation in the rat paw by approximately 75%. When shilajit was given orally at doses of 50–200 mg/kg twice a day to rats, significant dose-dependent decreases in the gastric ulcer index were observed, thus demonstrating significant anti-ulcerogenic activity. Additional studies involving dogs, frogs, and guinea pigs indicated that shilajit did not have significant activity with respect to the CNS, blood pressure, or skeletal muscle, and no antihistaminic activity.

In a study in rats, shilajit was shown to exhibit anti-ulcerogenic and anti-inflammatory activity when given at a dose of 100 mg/kg orally twice a day (Goel *et al.*, 1990). Shilajit decreased the gastric ulcer index and increased the carbohydrate/protein ratio, indicating an increased mucosal barrier. Furthermore, shilajit administration decreased carrageenan-induced acute pedal edema, granuloma pouch, and adjuvant-induced arthritis in these animals, indicating significant anti-inflammatory activity. Studies by Ghosal (2006) suggested that the anti-ulcerogenic effect of fulvic acids and biphenyls isolated from shilajit were due to protection of the gastrointestinal mucosa with less shedding of mucosal cells.

A number of early studies on the immunomodulatory effects of processed shilajit have been summarized by Ghosal (2006).These studies suggest that shilajit enhances the lytic potential of polymorphonuclear leukocytes. Studies in mice demonstrated that administration of 200–600 μg/dose resulted in marked morphological and phagocytotic changes in peritoneal macrophages (Bhaumik *et al.*, 1993; Ghosal *et al.*, 1995). These effects could at least in part explain the anti-inflammatory effects of shilajit.

The antioxidant activities of 3-hydroxy- and the 3,8-dihydroxy-DBPs, believed to be active constituents of shilajit and isolated therefrom, were demonstrated *in vitro* using five free radical scavenging assays (Battacharyya *et al.*, 2009a). When mice were treated IP with 20 mg of a mixture of the DBPs, the DBPs and their redox products were detected in hepatic mitochondria, the site of ATP and energy production.

Furthermore, when rats were treated orally with 3,8- DBP, CoQ10 was augmented in plasma and organs relative to the control animals, and *in vitro* erythrocyte membrane lipid peroxidation was inhibited (Battacharyya *et al.*, 2009a). These results suggest a mechanism for DBPs and shilajit to support the energy synthesizing ability of mitochondria and provide an explanation for the reported beneficial effects with respect to physical performance and relief from fatigue.

In a second study, Battacharyya *et al.* (2009b) examined the beneficial effects of processed shilajit (PrimaVie®) on energy status in forced swimming exercised mice. Mice were forced to swim daily for 7 days and received either the placebo or 30 mg shilajit/kg orally per day for the last 4 days. Swimming caused an 82% decrease in muscle ATP levels, while shilajit treatment almost doubled the ATP in muscle of mice forced to swim. Smaller effects of shilajit were observed with respect to ATP in brain and blood. Administration of CoQ10 resulted in a protection of muscle ATP similar to shilajit. When mice were treated with a combination of shilajit and CoQ10, muscle ATP levels were 2.44 times higher than untreated animals forced to swim. The primary biochemical function of CoQ10 is to synthesize ATP in the mitochondria. The results support the contention that shilajit can relieve fatigue and increasing energy and endurance.

The effects of a processed and standardized shilajit (25, 50 and 100 mg/kg/day for 21 days) on various stress factors in rats forced to swim 15 min per day for 21 days were assessed (Surapaneni *et al.*, 2012). The product contained 0.43% DBPs, 20.45% DCPs, and 56.75% fulvic acids. Shilajit reversed the forced swimming-

induced increase in immobility, decrease in climbing behavior, decrease in plasma corticosterone levels, and decrease in adrenal gland weight. Shilajit treatment also prevented forced swimming-induced mitochondrial dysfunction as evidenced by stabilizing complex chain enzymes and mitochondrial membrane potential. In addition, shilajit treatment also attenuated swimming-induced oxidative stress as indicated by decreases in nitric oxide and lipid peroxidation as well as increases in catalase and superoxide dismutase.

In an early study by Visser (1987), fulvic acids were shown to stimulate respiration in rat liver mitochondria and also increased oxidative phosphorylation when present in concentrations between 40 and 360 mg/L. These results are consistent with the above animal studies and provide mechanistic information regarding the increased energy and higher ATP levels.

The effects of shiljit on spermatogenesis and ovogenesis in rats were investigated (Park *et al.*, 2006). Shilajit administration daily for 6 weeks resulted in a significant increase in sperm count. Ovulation was induced in seven out of nine female rats in the shilajit group as opposed to three out of nine in the control group, indicating a questionable result in the female rats.

The antioxidant effects of shilajit have been demonstrated in several animal studies. Shilajit was shown to prevent lead-induced oxidative stress in a 6 week feeding study in chicks (Kumar *et al.*, 2010). Shilajit was included in the diet at 100 ppm. Antioxidant status was assessed based on glutathione peroxidase activity, glutathione reductase activity, catalase activity, glutathione content, and lipid peroxidation (thiobarbituric acid reactive substances).

In a study in mice, processed shilajit administration (0.1 and 1.0 mg/kg IP) resulted in significant inhibition of the development of tolerance to morphine (10 mg/kg IP twice daily) after 6 days of treatment (Tiwari *et al.*, 2001). Shilajit per se did not exhibit any analgesic activity in the mice. No explanation was provided for the observed effect.

Several studies have examined the anti-diabetic effects of shilajit. Bhattacharaya (1995) showed that the oral administration of 50 mg/kg and 100 mg/kg of a process and standardized shilajit attenuated streptozotocin-induced diabetes in rats. It also increased pancreatic islet superoxide dismutase, leading to a decrease in free radical production and accumulation. Kanikkannan *et al.* (1994) observed that a processed shilajit (1.0 mg/kg subcutaneously) prevented streptozotoxin-induced diabetes in rats. Furthermore, shilajit potentiated the hypoglycemic action of insulin.

Various studies have assessed some of the other hormonal effects of shilajit and its DBPs. In an early study, Schliebs *et al.* (1997) demonstrated that shilajit (40 mg/kg IP or 7 days) administration differentially affected cholinergic but not GABAergic or glutaminergic markers in rat brain as determined by brain slice histochemistry and autoradiography. The data suggested that shilajit preferentially affected cortical and basal forebrain cholinergic signal transduction cascade. An increase in the cholinergic signal transduction cascade could explain at least in part anecdotal reports of cognition and memory enhancing effects of shilajit.

In *in vitro* and *in vivo* studies involving rats, shilajit administration (400 μg/mL) exhibited an *in vivo* peripheral parasympathomimetic effect which can provide at least a partial explanation for the reported effects on spermatogenesis, as well as the anecdotal reports on overall fertility and libido (Kaur *et al.*, 2013). Furthermore, incubation of corpus cavernosum strips with shilajit (400 and 800 μg/mL) resulted in a concentration dependent relaxation of the strips and enhanced acetylcholine-mediated relaxation, suggesting an increased blood flow to the groin (Kaur *et al.*, 2013).

A study in mice has provided information on the ability of shilajit to exhibit glycine- and GABA-mimetic actions on the brainstem substantia gelatinosa neurons of the trigeminal subnucleus caudalis (Yin *et al.*, 2011). Mouse brainstem slices were incubated with shilajit in the presence of various receptor antagonists and channel blockers. Shilajit induced inward currents in a concentration-dependent manner. The results indicated that shilajit has central nervous system sedating ingredients and can mechanistically explain reports of skeletomuscular pain relief.

In an *in vitro* study, KU812 cells incubated with fulvic acid affected the expression of genes involved in signal transduction, cytokine–cytokine receptor interaction, and immune response pathways as well as cell adhesion molecule and IgE receptor β subunit responses (Motojima *et al.*, 2011). These results demonstrate the wide range of potential physiological effects that can be modulated by fulvic acids and help explain the immunomodulatory responses observed as a result of shilajit ingestion

DISCUSSION AND SUMMARY

In spite of the use of shilajit (moomiyo, mumie) for many years, relatively few peer-reviewed, human, controlled, and published research studies have been conducted. Many reports are poorly controlled, of an anecdotal, observational nature, and involve the use of non-standardized material. A growing number of studies in animals as well as *in vitro* systems are being published. Studies in both animals and humans indicate that the use of shilajit is safe and generally free of adverse effects. Published human and animal studies have indicated that shilajit increases spermatogenesis in infertile males. A human study demonstrated that shilajit when given at high (2000 mg/day) doses has beneficial effects with respect to blood lipids.

Several animal studies have clearly shown that shilajit exhibits antioxidant and anti-inflammatory activities, and supports production of ATP by the mitochondria. An unpublished human study has also provided support for the beneficial effects with respect to both ATP and CoQ10 production. Furthermore, in animal studies, DBPs exhibited mitochondrial protective effects which can explain the beneficial effects with respect to physical performance and relief from fatigue.

Animal studies have also examined the potential effects on various neurotransmitters and have demonstrated significant cholinergic and parasympathomimetic effects which can explain the potential benefits with respect to cognitive function and enhanced fertility.

The existence of unpublished studies on shilajit (moomiyo, mumie) within the USSR during the approximate time frame of 1960 through 1990 became known following the downfall of the USSR in 1991. Extensive

studies were reported to have been conducted on the physical and mental revitalizing effects of shilajit, and the product was purported to be widely used by USSR Olympic athletes as well as military special forces based on anecdotal reports on various websites and personal communication (Bucci, 2000; personal communication with Dr. N. Volkov).

Finally, it should be noted that products exist on the market that do not conform to the chemical composition of 'standard' shilajit and may be either adulterated or counterfeit. As a consequence, caution must be taken with respect to shilajit acquisition, and only processed and standardized products should be used. A need exists for further studies in animals and humans with processed and standardized shilajit preparations.

Conflict of Interest

The author has no conflicts of interest to report.

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