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INFLUENCE OF MUMIYO ON HEMOSTASIS DURING INDOMETHACIN-INDUCED PROSTAGLANDIN SUPPRESSION

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Abstract: This study aimed to evaluate the effect of mumiyo on blood coagulation under conditions of inhibited prostaglandin synthesis using indomethacin. Experiments were conducted on dogs, and blood coagulation was assessed by thromboelastography. Baseline coagulation parameters were recorded prior to drug administration. Indomethacin was administered intravenously at a dose of 5 mg/kg to inhibit prostaglandin synthesis. After the development of its effect, mumiyo extract was injected intravenously at a dose of 50 mg/kg. Thromboelastographic parameters were measured at various time intervals following each intervention. Indomethacin produced time-dependent alterations in thromboelastographic indices, characterized by transient procoagulant changes. Some parameters showed partial recovery within 30–60 minutes after administration. Subsequent administration of mumiyo modified these effects, resulting in a tendency toward normalization of coagulation parameters and indicating a mild hypocoagulant influence. Inhibition of prostaglandin synthesis by indomethacin leads to transient changes in blood coagulation. Mumiyo administration under these conditions exerts a moderate regulatory effect on hemostasis, suggesting that its anticoagulant action is at least partially independent of prostaglandin-mediated mechanisms.

Keywords: Mumiyo, Indomethacin, Prostaglandins, Blood coagulation, Thromboelastography, Hemostasis.

Introduction

According to the World Health Organization (WHO), traditional medicine (TM) encompasses a wide range of health practices that employ plant-, mineral-, and animal-derived remedies, used either individually or in combination for disease prevention, treatment, and the maintenance of well-being (1). TM systems are broadly categorized into several established traditions, including Traditional Persian Medicine (TPM), Traditional Arabic Medicine, Traditional Chinese Medicine (TCM), and Traditional Indian Medicine (Ayurveda) (2).

Within these traditional medical frameworks, Mumijo is classified as a herbomineral exudate with a long-standing ethnopharmacological heritage. It has been valued for centuries across various cultures, particularly in mountainous regions. Although most commonly associated with the Himalayan range of India (3,5), Mumijo is widely distributed throughout the former Soviet Union, including the Ural Mountains, Altai, Caucasus, Sayan Mountains, Baikal region, Kazakhstan, Uzbekistan, and Tajikistan. Additional deposits have been reported in China, Pakistan, Nepal, Afghanistan, and Tibet (6). Historically, Mumijo has been known by numerous names reflecting its widespread use across cultures, including *Shilajit* or *Silajita* in Indian traditions, *Rock Juice* in Tibetan medicine, *Mountain Conqueror* in Sanskrit, *Hajarul-Musa* or *Arak-al-Jebal* in Arabic, *Mumiyo* or *Mumnae* in Persian, and *μουμία* in Greek. Other designations include Mineral Resinous Bitumen, Mineral Wax, Jewish Bitumen, and Bragshun. Typically ranging in color from light to dark brown, Mumijo has been used for over 3,000 years as a rejuvenating agent and a powerful adaptogen (4).

The origin of Mumijo remains a subject of scientific debate, with three principal theories proposed: biological, geological, and bio-mineralogical. The biological hypothesis suggests that Mumijo originates from the decomposition of plant material or metabolic products of animals under specific environmental and physicochemical conditions. The geological theory considers it a product of prolonged geological processes, while the bio-mineralogical concept integrates both views, proposing that Mumijo results from interactions between organic precursors and the surrounding mineral matrix. Environmental factors such as local vegetation, geological substrate, soil characteristics, mineral composition, climate, altitude, and regional ecology significantly influence the chemical composition and therapeutic properties of Mumijo (9). Although samples from different regions exhibit similar physical characteristics, their chemical profiles vary considerably. In general, Mumijo consists of approximately 60–80% organic matter, 20–40% inorganic components, and trace elements such as iron, calcium, copper, zinc, magnesium, manganese, molybdenum, and phosphorus (10).

Classical medical literature extensively documents the therapeutic applications of Mumijo. In the 10th century, the Persian physician Ahvazi described its medicinal benefits in *Kamāl as-Sanā'a*, recommending its use for cold-type headaches, hemoptysis, asthma, and facilitating the expulsion of retained fetuses. Avicenna, in *The Canon of Medicine*, regarded Mumijo as a potent neurotonic, capable of strengthening the brain, enhancing reproductive capacity, and treating various systemic disorders. Similarly, in the 12th century, Jurjani's *Zakhire Khwārizmshāhi* emphasized its efficacy in inflammatory conditions, ulcers, urinary dysfunction, and prostate diseases (7).

Across different traditional healing systems, Mumijo has been administered in diverse dosage forms for the management of numerous conditions, including urinary tract disorders, jaundice, gallstones, gastrointestinal disturbances, splenomegaly, epilepsy, allergic reactions, neurological diseases, chronic bronchitis, tuberculosis, dermatological disorders such as eczema, anemia, and diabetes (11). Despite its broad therapeutic application, concerns regarding fungal contamination and the potential presence of mycotoxins represent a significant challenge to its widespread clinical use and global acceptance (12).

Traditional practitioners continue to attribute a wide range of therapeutic properties to Mumijo, including benefits in reduced libido, nephrolithiasis, musculoskeletal pain, bone fractures, osteoarthritis, spondylitis, edema, hemorrhoids, age-related degeneration, wound healing, metabolic disorders, and weight regulation (9). Contemporary pharmacological studies have provided scientific support for several of these traditional claims, identifying anti-inflammatory, antioxidant, antimutagenic, and immunomodulatory activities largely associated with its fulvic acid (FA) and humic acid (HA) content. These bioactive compounds have drawn attention to Mumijo as a potential chemopreventive agent (10). Experimental studies further indicate that Mumijo can reduce blood glucose levels, improve lipid metabolism in animal models (13), stimulate nucleic acid synthesis, enhance mineral transport to bone and muscle tissues (6), and increase both diuresis and natriuresis, thereby supporting its traditional use in renal and urinary disorders (14).

Materials and Methods

The experiments were designed to investigate the involvement of prostaglandins in the effects of mumiyo on blood coagulation. Indomethacin, a known inhibitor of prostaglandin synthetase, was used to suppress endogenous prostaglandin synthesis.

The study was conducted on 19 adult dogs. Blood coagulation parameters were assessed using thromboelastography. Baseline thromboelastographic values were recorded prior to drug administration.

Indomethacin was administered intravenously at a dose of 5 mg/kg after dissolution in dimethyl sulfoxide (DMSO). Control experiments using DMSO alone confirmed that the solvent had no effect on coagulation parameters. Thromboelastographic measurements were repeated at various time intervals following indomethacin administration to assess its effect on hemocoagulation.

After the development of the pharmacological effect of indomethacin (60–90 minutes post-injection), an extract of Alai mumiyo was administered intravenously at a dose of 50 mg/kg. Subsequent thromboelastographic recordings were performed at different time points to evaluate changes in blood coagulation parameters.

Thromboelastographic indices analyzed included reaction time (R), clot formation time (K), α-angle, maximum amplitude, and other standard parameters. Data were analyzed to determine the influence of prostaglandin synthesis inhibition on the coagulation-modulating effects of mumiyo.

Results

Administration of indomethacin produced pronounced time-dependent changes in thromboelastographic parameters compared with baseline values (Table). At 15–20 minutes after indomethacin injection, Parameter 1 decreased, while Parameter 2 and Parameter 6 increased, indicating a shift toward increased coagulation activity. Moderate reductions were also observed in Parameters 3–5.

Table 1. Effect of Hamzaabad Mumiyo Extract on Selected Thromboelastographic Parameters in Dogs under Indomethacin Treatment (n = 10)

Experimental condition	Parameter 1	Parameter 2	Parameter 3	Parameter 4	Parameter 5	Parameter 6
Baseline (control)	42.2 ± 5.9	13.0 ± 1.7	52.5 ± 4.6	77.9 ± 7.3	102.4 ± 8.9	139.8 ± 18.5
Indomethacin, 15–20 min	36.2 ± 5.8	22.5 ± 6.9	49.5 ± 9.1	66.0 ± 7.6	98.4 ± 11.4	170.4 ± 16.6
Indomethacin, 30–60 min	22.3 ± 1.5	13.4 ± 1.4	51.5 ± 5.9	70.0 ± 4.7	86.3 ± 7.0	105.5 ± 7.4
Mumiyo + indomethacin, 20 min	31.1 ± 5.3	20.2 ± 6.5	48.5 ± 12.4	82.2 ± 9.0	104.5 ± 11.7	135.8 ± 10.0
Mumiyo + indomethacin, 40 min	24.7 ± 4.6	20.7 ± 7.3	43.5 ± 9.1	77.0 ± 7.3	99.3 ± 11.0	122.7 ± 10.0

Statistically significant differences ($p < 0.05$) compared with baseline values.

At 30–60 minutes, Parameter 1 reached its lowest value, and Parameter 5 decreased further compared with baseline. In contrast, Parameter 6 declined toward control levels, suggesting partial recovery of coagulation parameters over time following indomethacin administration.

Administration of mumiyo in animals pretreated with indomethacin altered these changes. Twenty minutes after mumiyo injection, Parameter 1 increased relative to the indomethacin 30–60 min values, and Parameters 4 and 5 exceeded baseline levels. Parameter 6 decreased compared with the peak values observed after indomethacin alone. At 40 minutes after mumiyo administration, most parameters showed a tendency to return toward baseline values.

Overall, indomethacin induced transient procoagulant alterations in thromboelastographic indices, whereas mumiyo administration on this background resulted in partial normalization of these parameters, indicating a mild hypocoagulant or regulatory effect on blood coagulation.

Discussion

The present study demonstrates that inhibition of prostaglandin synthesis with indomethacin leads to distinct, time-dependent alterations in thromboelastographic parameters in dogs. Shortly after indomethacin administration, several indices shifted toward a hypercoagulable state, which is consistent with the known role of prostaglandins—particularly prostacyclin—in maintaining normal antithrombotic balance. Suppression of prostaglandin synthesis is therefore likely to reduce endogenous anticoagulant mechanisms and promote coagulation.

The subsequent partial normalization of thromboelastographic parameters observed 30–60 minutes after indomethacin injection may reflect compensatory regulatory mechanisms within the hemostatic system. These findings suggest that the procoagulant effect of indomethacin is transient and subject to physiological counter-regulation.

Administration of mumiyo on the background of prostaglandin synthesis inhibition modified the indomethacin-induced changes. Several thromboelastographic parameters shifted toward baseline values, and some indices demonstrated changes consistent with a mild hypocoagulant effect. This suggests that the influence of mumiyo on blood coagulation is not solely dependent on prostaglandin-mediated pathways and may involve additional mechanisms, such as direct effects on platelet function, plasma coagulation factors, or fibrinolytic activity.

Taken together, these results indicate that mumiyo is capable of modulating coagulation even under conditions of suppressed prostaglandin synthesis, although its effect appears moderate rather than pronounced.

Conclusion

Indomethacin-induced inhibition of prostaglandin synthesis results in transient procoagulant changes in thromboelastographic parameters. Administration of mumiyo under these conditions partially attenuates these changes and promotes a tendency toward normalization of blood coagulation indices. These findings suggest that mumiyo exerts a mild regulatory, predominantly hypocoagulant effect on hemostasis that is at least partly independent of prostaglandin-mediated mechanisms.

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