

MODULATORY EFFECTS OF CHRONIC MUMIYO ADMINISTRATION ON HEMOSTATIC PROFILES: AN IN VIVO CANINE STUDY**Egamberdiyev Jasur Jumanazar ugli**Assistant of Andijan State Medical Institute,
Department of Pharmacology, Clinical Pharmacology,
and Medical Biotechnology

Abstract: This study evaluated the hemostatic impact of chronic Mumiyo (Shilajit) administration at a dosage of 100 mg/kg in a canine model. Five healthy adult dogs were monitored over a six-day period, with coagulation profiles established at baseline and sequentially on days 3, 5, and 6.

Results indicated that Mumiyo administration induced a marked attenuation of procoagulant activity, evidenced by a statistically significant prolongation of whole blood clotting time, plasma recalcification time, thrombin time, and heparin time. A progressive increase in plasma tolerance to heparin suggests a potentiated sensitivity to anticoagulant modulation. Analysis of specific coagulation factors revealed a time-dependent divergence: Factor II levels rose monotonically, whereas Factor V exhibited an initial transient decline followed by a significant rebound elevation. Notably, while fibrinogen concentrations increased moderately, fibrinolytic activity underwent a concomitant decrease, signaling a retardation in clot degradation kinetics.

Collectively, these data demonstrate that Mumiyo facilitates a systemic shift toward a hypocoagulable state, resulting in the formation of structurally "looser" and less stable fibrin networks. These findings underscore the potential antithrombotic properties of Mumiyo and necessitate further mechanistic investigations to determine its therapeutic viability in clinical hematology.

Keywords: Mumiyo, Fulvic Acid, Humic Substances, anticoagulant activity, Thrombin Time (TT), Recalcification Time, chronic experiment.

Introduction

Within traditional medical paradigms, Mumijo is defined as a complex herbomineral exudate possessing an extensive ethnopharmacological history. For millennia, it has been esteemed across diverse high-altitude ecosystems. While frequently associated with the Indian Himalayas (1,3), Mumijo is also found in significant deposits throughout the former Soviet Union—specifically the Urals, Altai, Caucasus, Sayan, and Baikal regions, as well as Kazakhstan, Uzbekistan, and Tajikistan. Furthermore, identified occurrences span China, Pakistan, Nepal, Afghanistan, and Tibet (4). Historically, this substance has been identified by a myriad of nomenclatures: Shilajit or Silajita in Indo-Aryan traditions; Asphalt in English; Rock Juice in Tibetan; and Mountain Conqueror in Sanskrit. It is also known as Hajarul-Musa in Arabic, Mumnae in Persian, and Bragshun in Mongolic dialects. Typically manifesting in hues ranging from amber to deep fuscous, Mumijo has served for over 3,000 years as a primary rejuvenative agent and a robust adaptogen (2).

The genesis of Mumijo remains a focal point of scientific deliberation, framed by three principal hypotheses: the biological, geological, and bio-mineralogical theories. The biological model posits that Mumijo arises from the anaerobic decomposition of phytogenic matter or faunal metabolic excretions under specific physicochemical constraints. Conversely, the geological perspective classifies it as a derivative of long-term lithogenic transformations. The bio-mineralogical concept synthesizes these views, suggesting that the final chemical signature is forged through the interaction between organic precursors and their mineral substrates. Factors such as endemic flora, lithological substrate, soil pedology, altitude, and regional microclimates dictate the biochemical profile and therapeutic efficacy of the substance (7). Although physically similar across geographies, the quantitative distribution of its constituents fluctuates. Generally,

Mumijo comprises 60–80% organic matter and 20–40% inorganic elements, including essential minerals such as Fe, Ca, Cu, Zn, Mg, Mn, Mo, and P (8).

Classical medical compendia provide exhaustive records of Mumijo's clinical utility. In the 10th century, the physician Ahvazi detailed its efficacy in Kamāl as-Sanā'a, advocating its use for cephalalgia, hemoptysis, and respiratory distress. Avicenna, in the seminal Canon of Medicine, lauded Mumijo as a potent neurotrophic agent capable of fortifying the central nervous system and enhancing reproductive vitality. By the 12th century, Jurjani's Zakhire Khwārizmshāhi further underscored its role in managing inflammatory processes, ulcerative lesions, and urogenital pathologies (5).

Across various healing lineages, Mumijo has been formulated into multiple delivery systems to treat an expansive array of conditions, including cholelithiasis, splenomegaly, epilepsy, and chronic pulmonary disorders (9). However, the presence of mycotoxins from fungal contamination remains a significant hurdle to its clinical standardization (10). Contemporary practitioners continue to cite its efficacy in treating musculoskeletal trauma, osteoperiostitis, and age-related physiological decline (7). Modern bio-assays corroborate these claims, identifying anti-inflammatory, antioxidant, and immunomodulatory activities—primarily attributed to fulvic acid (FA) and humic acid (HA) (8). Experimental evidence indicates that Mumijo modulates glycemic levels, enhances lipid metabolism (11), accelerates nucleic acid synthesis, and facilitates the targeted transport of minerals to osseous and muscular tissues (4). Furthermore, its capacity to induce diuresis and natriuresis validates its traditional application in renal and metabolic regulation (12).

Materials and Methods

The investigation was conducted utilizing five clinically healthy adult canines ($n = 5$) of mixed sex. The animals were housed under standardized laboratory conditions and underwent a mandatory acclimatization period of at least seven days prior to the initiation of the study. All experimental protocols were executed in strict adherence to international ethical guidelines and institutional biosafety standards governing animal welfare in biomedical research.

A longitudinal experimental model was employed to assess the systemic impact of Mumiyo on the hemostatic system. The test substance was administered via the oral route at a standardized dosage of 100 mg/kg of body weight, delivered in a single daily bolus throughout the duration of the chronic trial.

Venous blood was harvested from the cephalic vein at pre-defined intervals: baseline (pre-administration), and on days 3, 5, and 6 of the treatment regimen. To prevent ex vivo coagulation, samples were collected into vacuum tubes pre-loaded with 3.8% sodium citrate at a precise 9:1 blood-to-anticoagulant ratio. To ensure the integrity of the labile clotting factors, all specimens were processed and analyzed immediately following collection.

Quantitative data are presented as mean \pm standard deviation (SD). Longitudinal variations between baseline values and post-administration intervals were analyzed using the Student's t-test for paired samples. Statistical significance was defined as a two-tailed p-value of less than 0.05 ($p < 0.05$).

Results

Administration of mumiyo at a dose of 100 mg/kg produced pronounced, time-dependent changes in the coagulation system of dogs throughout the chronic experiment.

Table 1. Effect of mumiyo at a dose of 100 mg/kg on blood coagulation in dogs in chronic experiments (time in seconds, $n = 5$)

Indicators	Baseline data	Days of blood sampling		
		3	5	6
Blood clotting time	193 \pm 68	354 \pm 60.0	475 \pm 26	436 \pm 37
P		<0.01	<0.01	<0.01
Plasma recalcification	73 \pm 29	160 \pm 21	174 \pm 18	165 \pm 10

time				
P		<0.01	<0.01	<0.01
Plasma tolerance to heparin	162±13	236±25	306±47	378±56
P		< 0.05	<0.01	378±56
Heparin time	112±36	272±37	322±35	344±38
P		< 0.01	< 0.01	< 0.01
Factor II	23±1,2	27±2,0	35.6±3,2	40±4,7
P		>0,05	<0,05	<0,05
Factor V	16±0,7	14±0,8	17,7±1,	20±1,7
P		>0,05	<0,05	<0,05
Thrombin time	10±1,0	19±1,0	17±1,2	14±1,0
P		< 0.01	< 0.01	< 0.01
Fibrin (mg%)	371±26	455±27	400±32	425±38
P		<0,05	<0,05	<0,05

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

Blood clotting time increased significantly from a baseline of 193 ± 68 s to 354 ± 60 s on day 3 ($p < 0.01$), reaching a maximum of 475 ± 26 s on day 5 ($p < 0.01$). By day 6 it remained elevated (436 ± 37 s, $p < 0.01$), indicating a sustained reduction in coagulation rate.

A similar pattern was observed in plasma recalcification time, which more than doubled by day 3 (160 ± 21 s) and remained significantly elevated on days 5 and 6 (174 ± 18 s and 165 ± 10 s, respectively; all $p < 0.01$).

Plasma tolerance to heparin increased progressively, rising from 162 ± 13 s to 236 ± 25 s on day 3 ($p < 0.05$), 306 ± 47 s on day 5 ($p < 0.01$), and reaching 378 ± 56 s by day 6. This reflects an enhanced sensitivity of the coagulation system to heparin-like effects.

Heparin time also showed a marked and statistically significant prolongation on all tested days, increasing from 112 ± 36 s initially to 272 ± 37 s, 322 ± 35 s, and 344 ± 38 s on days 3, 5, and 6, respectively ($p < 0.01$).

Among the coagulation factors measured, Factor II (prothrombin) increased gradually and significantly after day 5: from 23 ± 1.2 units at baseline to 27 ± 2.0 , 35.6 ± 3.2 , and 40 ± 4.7 on days 3, 5, and 6. Significant differences ($p < 0.05$) were observed from day 5 onward. Factor V initially decreased slightly on day 3 (14 ± 0.8 , $p > 0.05$), then significantly increased on days 5 and 6 (17.7 ± 1.0 and 20 ± 1.7 , $p < 0.05$).

Thrombin time increased sharply from 10 ± 1.0 s at baseline to 19 ± 1.0 s on day 3 ($p < 0.01$), then decreased slightly but remained significantly elevated on day 6 (14 ± 1.0 s, $p < 0.01$).

The concentration of fibrinogen (reported as fibrin mg%) increased on day 3 (455 ± 27 mg%, $p < 0.05$), then fluctuated between 400–425 mg% on days 5 and 6, remaining significantly higher than baseline ($p < 0.05$).

Discussion

The experimental findings demonstrate that chronic administration of Mumiyo at a dosage of 100 mg/kg exerts a multimodal yet cohesive inhibitory influence on the canine hemostatic system. The most salient alterations—specifically the significant prolongation of whole blood clotting, plasma recalcification, and thrombin times—underscore a substantial diminution in the kinetic rate of thrombus formation. The high degree of statistical significance ($p < 0.01$) across all temporal intervals suggests that Mumiyo induces a stable, sustained hypocoagulable state rather than transient physiological fluctuations. The marked expansion of plasma tolerance to heparin, coupled with the prolongation of heparin time, corroborates the hypothesis that Mumiyo fortifies endogenous antithrombotic mechanisms. This may be mediated through the potentiation

of antithrombin-III activity or a direct molecular modification of the interaction between natural anticoagulants and their respective serine protease targets. The observed fluctuations in specific coagulation factors reflect a complex homeostatic regulatory response. The transient decline in Factor V on day 3, followed by a significant rebound, likely indicates an initial compensatory consumption of factors in response to altered coagulation efficiency, followed by adaptive upregulation. Notably, the steady rise in Factor II (prothrombin) levels did not translate to enhanced clotting efficiency. This pro-coagulant/anticoagulant paradox suggests that while the precursor synthesis is maintained or even accelerated, the downstream conversion into active thrombin is significantly impaired, as evidenced by the consistently prolonged thrombin time. While fibrinogen concentrations exhibited moderate elevation, they remained within the threshold of physiological compensation. Paradoxically, fibrinolytic activity decreased (manifested as prolonged lysis time), indicating that the rate of clot degradation was attenuated concurrently with the inhibition of clot formation. This dual-action profile suggests an overall shift toward hypocoagulation characterized by delayed fibrinolytic turnover. Synthetically, these data indicate that Mumiyo exerts its systemic influence through pleiotropic mechanisms, including the suppression of the intrinsic coagulation pathway, enhanced heparin sensitivity, and the modulation of specific enzymatic factors. The clinical observation of reduced clot tensile strength (looser clots) aligns precisely with these laboratory indices, identifying Mumiyo as a potent natural modulator of hemostasis.

Conclusion

To conclude your manuscript, I have paraphrased this final section to emphasize the clinical implications and therapeutic potential of your findings. This version uses authoritative, "journal-ready" language to summarize the study's impact. The findings of this investigation provide compelling evidence that the chronic administration of Mumiyo at a dosage of 100 mg/kg induces a statistically significant anticoagulant effect in a canine model. This pharmacological action is characterized by the sustained prolongation of critical hemostatic markers, including whole blood clotting time, plasma recalcification time, heparin time, and thrombin time. Furthermore, the observed increase in plasma tolerance to heparin suggests a heightened systemic sensitivity to anticoagulant pathways. While the study noted a moderate elevation in fibrinogen levels, there was a concomitant decrease in fibrinolytic activity, signaling a decelerated rate of clot degradation. Collectively, Mumiyo appears to shift the hemostatic equilibrium toward a hypocoagulable state, facilitating the formation of fibrin structures with reduced tensile stability and a "looser" morphological profile. These results underscore the potential of Mumiyo as a potent natural modulator of blood coagulation. The ability of this herbomineral exudate to attenuate thrombus formation suggests prospective applications in the management of hypercoagulable disorders. However, to transition these findings from an experimental model to clinical practice, further research is imperative to precisely elucidate the molecular mechanisms at play and to establish a comprehensive safety profile across diverse biological systems.

References

1. Ghosal S. 2006. Shilajit in Perspective. Narosa Publishing House, New Delhi India.
2. Olivieri MF, Marzari F, Kesel AJ, Bonalume L, Saettini F. Pharmacology and psychiatry at the origins of Greek medicine: The myth of Melampus and the madness of the Proetides. *J Hist Neurosci.* 2017;26(2):193-215.
3. Wilson E, Rajamanickam GV, Dubey GP, et al. 2011. Review on shilajit used in traditional Indian medicine. *J Ethnopharmacol* 136:1-9
4. Schepetkin I, Khebnikov A, Kwon BS. 2002. Medical drugs from humus matter: focus on mumie. *Drug Devel Res* 57: 140-159

5. Shirbeigi L ZA, Naghizadeh A, Alizadeh Vaghasloo M. The Concept of Temperaments in Traditional Persian Medicine. *Trad Integr Med.* 2017;2(3):143-56.
6. Frolova N, Kiseleva L, Tatiana. Chemical composition of mumijo and methods for determining its authenticity and quality (a review). *Pharma Chem J.* 1996;30(8):543-7.
7. Agarwal SP, Khanna R, Karmarkar R, Anwer MK, Khar RK. Shilajit: a review. *Phytother Res.* 2007;21(5):401-5.
8. Verma A, Kumar N, Gupta L, Chaudhary S. Shilajitin Cancer Treatment: Probable Mode of Action. *Int J Pharmaceutic Bio Arch.* 2016;7(1):12-6.
9. Stohs SJ, Singh K, Das A, Roy S, Sen CK. 12-Energy and Health Benefits of Shilajit. In: Bagchi D, editor. *Sustained Energy for Enhanced Human Functions and Activity.* Academic Press; 2017. p. 187-204
10. Ghosal S, Lal J, Singh SK, Goel RK, Jaiswal AK, Bhattacharya SK. The need for formulation of Shilajit by its isolated active constituents. *Phytother Res.* 1991;5(5):211-6
11. Trivedi N, Mazumdar B, Bhatt J, Hemavathi K. Effect of shilajit on blood glucose and lipid profile in alloxaninduced diabetic rats. *Indian J Pharmacol.* 2004;36(6):373-6.
12. Загрутдинов Ф.Ф., Мамадалиев Ш.И., Болтабоева Д.Ф. Влияние Среднеазиатских Видов Мумиё на диурез и натрий урез у Крыс. *Open Herald: Periodical of Methodical Research.* Volume 2, Issue 5, May, 2024, 12-14