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The Application of Biologically Active Components Derived from Mineral, Synthetic, Phyto- and Organic Sources for Developing Local Hemostatic Agents: Historical Traditions and Contemporary Advancements

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Abstract

The present paper aims to provide an overview of the use of biologically active components derived from mineral, synthetic, phyto-, and organic sources in the development of local hemostatic agents. The study highlights the historical and contemporary use of these agents in medical practice, and examines the scientific evidence supporting their efficacy.

Hemostasis, the process of stopping bleeding, is a critical component of surgical and medical procedures. Local hemostatic agents are widely used to achieve hemostasis in a

targeted and controlled manner, thereby minimizing the risk of complications associated with bleeding.

The use of biologically active components derived from various sources, including minerals, synthetic materials, plants, and organic compounds, has a long history in the development of hemostatic agents. These components can act through various mechanisms, such as inducing platelet aggregation, activating the coagulation cascade, or promoting the formation of blood clots.

Recent advances in biotechnology and nanotechnology have led to the development of novel hemostatic agents with improved properties, such as enhanced biocompatibility, targeted delivery, and controlled release. These agents have the potential to revolutionize hemostasis in surgical and medical procedures, and improve patient outcomes.

Overall, the study highlights the importance of biologically active components derived from mineral, synthetic, phyto-, and organic sources in the development of local hemostatic agents. The review of historical and contemporary use of these agents underscores their continued relevance in medical practice, while recent advances in technology offer exciting new possibilities for future development.

After a thorough review of domestic and foreign literature, the development team used adsorbing materials from biologically active components of mineral, synthetic, phyto-, and organic origin to create a hemostatic powder known as "PLANTOR." The active components of PLANTOR include aerosol, carrageenan of a special brand, and a specific mixture of medicinal vegetable oils, which have a special sorption effect. Due to the well-selected composition of the product, PLANTOR forms a blood clot in the wound through a biophysical process of liquid absorption. Notably, PLANTOR does not contain procoagulant minerals or nanoparticles that could remain in the human body, and therefore does not belong to means with a chemical or biochemical mechanism of action.

Based on the above, it is possible to recommend the hemostatic agent-powder "PLANTOR" of the trade mark "PLANTOR tm" and "Dr. Sokolovskiy R" of the manufacturer "Medpro Nutraceuticals" (Latvia) by order of LLC "Plantor" (Ukraine, Dnipro), the author and owner of the developed technology of the hemostatic agent - powder "PLANTOR" (TU U 20.4-44827581-001:2022) as an auxiliary means of revitalization, local coagulation, treated wound surfaces during emergency medical care for external bleeding.

Keywords: **bleeding; hemostatic agents; adsorbing materials; natural hemostatics**

Introduction. Prolonged bleeding resulting from emergency, trauma, or combat injuries remains a major preventable cause of death, both during peacetime and combat scenarios (Malik et al., 2021; Schauer et al., 2019). Consequently, the development and implementation of effective methods for stopping bleeding are crucial. Several methods and means have been proposed for temporarily stopping critical external bleeding, including the use of a hemostatic tourniquet, compression bandage, wound tamponade, and contact hemostatic agents. However, none of these approaches is universal (Rass, 2021; PGR Teixeira et al., 2018; Palmer, 2022; Sung et al., 2021).

An analysis of the known methods and means for temporarily stopping bleeding shows that medical means, such as contact hemostatics, cannot fully replace final surgical hemostasis, but are highly effective, especially when used in combination with mechanical methods for achieving hemostasis, during the provision of emergency pre-medical and medical care (Christopher et al., 2021; Wang et al., 2019; Thompson, 2019).

In light of Russian aggression against Ukraine, we conducted an analysis of medical examination data of the wounded and causes of death in hostilities, which revealed massive blood loss as one of the leading causes of fatalities (Mazuchowski et al., 2020; Kotwal et al., 2018; Howard et al., 2019).

As a result, a sudden shortage of hemostatic agents arose, which neither military medicine nor the volunteer movement could address adequately. Furthermore, foreign hemostatics often caused adverse effects, such as allergic reactions and burns to wound and mucous tissues of the eyes. Thus, a group of Ukrainian scientists and volunteers undertook the task of creating a local hemostatic agent (Hemostop) that would not have such defects, enabling it to remain in the wound for an extended period, even if evacuation of the victim was difficult or impossible.

Hemostatic biologically active components

After a comprehensive review of domestic and foreign literature, adsorbing materials derived from biologically active components of mineral, synthetic, phyto- and organic sources with a broad spectrum of action served as the basis for the hemostatic agent (Huang et al., 2020; Zhang et al., 2018; Xiang-Fei et al., 2023). However, the primary challenge in selecting the components for the tool was that most scientific studies lacked significant practical benefit for clinical implementation. While laboratory studies on rats demonstrated the mechanisms of action of the components, they did not account for regulatory guidelines on the production of the drug for clinical use. Additionally, most researchers did not address the issue of the sterility of hemostatic agents. Hence, our group of scientists conducted appropriate microbiological

studies to ensure the sterility of the hemostatic agent, leading to the search for biologically active components of mineral, synthetic, phyto- and organic sources with a broad spectrum of action capable of achieving the required level of microbial contamination control for the drug.

However, the challenges of creating the hemostatic agent did not end with its formulation. Firstly, it became apparent that scaling up for industrial production necessitated a modification of the recipe to incorporate different biologically active components and their ratios. Secondly, the developers set an ambitious goal of organizing industrial production of the hemostatic agent in accordance with Good Manufacturing Practice (GMP) standards. However, due to the military situation in Ukraine, it was challenging to achieve this objective domestically. Consequently, the initiative group sought assistance from their Latvian colleagues, who supported and organized the production of the pharmacotherapeutic agent under GMP conditions at "Medpro Nutraceuticals" (Latvia) for PLANTOR LLC (Ukraine, Dnipro), the primary developer of the "PLANTOR tm" aid for providing emergency medical assistance in cases of external bleeding.

To manufacture the hemostatic agent in the European Union under GMP production conditions, an international team of scientists had to conduct extensive research. It was discovered that some of the biologically active components in the formulation had reservations regarding their use on the European market. Consequently, the composition of the hemostatic agent had to be modified to meet European standards and requirements, and technical conditions for the production of the hemostatic agent - PLANTOR powder (TU U 20.4-44827581-001:2022) - had to be developed. The team expresses its gratitude to the experts at Zaporizhzhya Medical University for their invaluable contributions to this effort.

Thus, a challenging journey culminated in the creation of a unique tool, "PLANTOR tm," using highly effective adsorbent materials from biologically active components of mineral, synthetic, phyto-, and organic origin. Its most significant feature is the ability to stop bleeding quickly, including dangerous cases, without any potential complications during surgery or the rehabilitation period. The demand for such tools is high, particularly in modern combat scenarios, where timely and effective bleeding control saves the lives of soldiers. The tool must meet specific requirements, such as having antiseptic properties to prevent infectious complications and ease of use, including self-administration.

The hemostatic powder "PLANTOR ^{TM} " operates through a special sorption effect from biologically active components of phyto- and organic origin, including aerosol, carrageenan of a specific brand, and mixtures of medicinal vegetable oils. The product's well-designed composition results in the biophysical process of liquid absorption, causing "PLANTOR ^{TM}" to

form a blood clot in the wound. Notably, "PLANTOR ™" does not contain procoagulant minerals or nanoparticles that may persist in the human body, and thus, it does not belong to chemical or biochemical mechanisms of action.

PLANTOR ™ powder Clinical validation

The clinical validation of the hemostatic agent, PLANTOR powder (TU U 20.4-44827581-001:2022), was conducted at the pre-hospital and early hospital stages of medical care provision, in compliance with the recommendations of the product owner, PLANTOR LLC (Ukraine, Dnipro). Emergency medical assistance was administered to 78 patients with isolated and polytrauma, who exhibited critical (pulsating nature of blood flow, rapidly expanding pool of blood on the surface on which the victim is located, and intense blood soaking of clothing in the wound area) and non-critical bleeding. The average age of the patients was 43.5 (27; 58) years, with a body weight of 78.7 (64.3; 94.6) kg.

The hemostatic agent-powder "PLANTOR" (TU U 20.4-44827581-001:2022) was evaluated for clinical efficacy in emergency medical care provision for victims with trauma in pre-hospital (emergency medical aid teams) and early hospital (emergency medical aid department) settings. A total of 78 victims with isolated trauma and polytrauma were treated for critical and non-critical bleeding according to the recommendations of the product owner LLC "Plantor" (Ukraine, Dnipro). The average age of the victims was 43.5 (27; 58) years, and the average body weight was 78.7 (64.3; 94.6) kg.

Upon contact with blood, "PLANTOR" powder absorbed plasma and formed a blood clot that swelled and stuck together into a single thick mass, which prevented further bleeding and significantly reduced blood loss. The microbiological purity and antiseptic component of the product effectively prevented the development of wound infections, and it did not delay regeneration or natural wound healing. The product was easily washed out of the wound during surgical treatment and did not cause anaphylaxis, inflammatory complications, or thermal or chemical burns. Furthermore, it showed efficacy in stopping bleeding under conditions of hypothermia and in the presence of antiaggregants and anticoagulants.

"PLANTOR" powder was found to be effective in treating critical and non-critical external bleeding, including all bleeding wounds, lacerations, sores, and cuts. The product can be used by pouring quantum satis into the victim's wound and immediately tamponing the wound for 2-3 minutes in cases of critical external bleeding. For non-critical external bleeding, the wound should be tightly bandaged after pouring the product into the wound.

Contraindications to the use of "PLANTOR" powder include traumatic amputation of a limb, bleeding from penetrating wounds of the torso and abdomen, and internal bleeding. Based

on these findings, "PLANTOR" powder can be recommended for use in emergency medical care for victims with trauma to prevent bleeding and promote wound healing.

The mechanism of action and application procedure for "PLANTOR" is straightforward: simply tear open the package, pour the contents onto the wound, and tightly bandage the area. In cases of severe, profuse bleeding (such as arterial bleeding), "PLANTOR" should be used in conjunction with mechanical hemostasis methods (such as tourniquets or hemostatic tourniquets). When necessary, more than one dose can be used for heavy bleeding. Due to its compact size, light weight, and rapid action, "PLANTOR" can be used in any emergency situation, even in non-sterile conditions, as it has an antiseptic effect. This innovative product is capable of providing beneficial effects even in extreme conditions.

Conclusion and perspectives

Based on the above information, we recommend the use of the hemostatic agent-powder "PLANTOR," which is produced by "Medpro Nutraceuticals" (Latvia) on behalf of LLC "Plantor" (Ukraine, Dnipro), the owner and developer of the "PLANTOR" technology. This hemostatic agent-powder (TU U 20.4-44827581-001:2022) is recommended as an auxiliary revitalization tool for local coagulation and wound surface treatment during emergency medical care for external bleeding.

Currently, Ukraine is in urgent need of hemostatic agents, and the "PLANTOR" tool has the potential to save the lives of both military and civilian personnel in field conditions where evacuation to a hospital is difficult. These agents quickly stop bleeding in challenging situations, making their presence crucial.

The "PLANTOR" hemostatic agent-powder is a remarkable example of combining Ukrainian folk medicine traditions, the knowledge and expertise of folk healers, the Cossack characters of Zaporizhzhya Sich, and contemporary researchers, production organizers, and volunteers. In a short amount of time, they managed to develop and organize the production of such an essential tool.

The hemostatic agent "PLANTOR" was developed through volunteer efforts and is currently being provided to Ukrainian military brigades and TRO at no cost until they are fully supplied. We express our sincere gratitude to the Academy of Technological Sciences of Ukraine, the Official Representation of the International Nobel Information Center in Ukraine, the Charity Fund "Volunteers of the World," LLC "Sokolovsky - Fortuna," Dnipro Medical Institute of Traditional and Non-Traditional Medicine, Zaporizhzhia State Medical University, and specialists from the University of Pharmacy in Kharkiv for their scientific and organizational support and advice in the development of this important tool.

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