



UniPharma
Group

PATHELEN HYBRID®

**HYDROPHILIC / HYDROPHOBIC
NANOCOMPOSITION FOR WOUND
CARE AND METHOD OF ITS
MANUFACTURING AND USE**

NANO TECHNOLOGY

Aerosil A-300 Pharma

Pathelen Health Care AG (PHC) have invented nanocomposition Pathelen® for local treatment of purulent wound based on Silics - preparation synthesised at the Institute of Surface Chemistry in Kyiv, Ukraine (from Silica - SiO₂ and ICS - Institute Chemistry Surface). The substance for the production of Silica is highly dispersed silica - **Aerosil A-300 Pharma**.

Aerosil is obtained by high-temperature hydrolysis of silicon tetrachloride SiCl₄. After three consecutive technological stages, a product is formed with a specific surface area of $300 \pm 30 \text{ m}^2 / \text{g}$. This is if you scatter of 1 tbsp. of the powder with the layer in one particle, then the surface area will be like two volleyball courts!

The surface of the particles is covered with hydroxyl groups, so highly dispersed silica, crushed to nanoparticles (1-4 nm) acquires these properties:

- **high hydrophilicity** (900% total, 500% – during first 24 hrs.
- **protein-adsorbing ability**, which is three orders of magnitude superior to all known medical sorbents. An important indicator is the sorption rate of protein toxins. Silica only needs 10 minutes to fully connect proteins.
- **the ability to connect microorganisms** (adsorption of microorganisms = $3 \text{ billion} \times 10^9$ microbial bodies per 1 g of Silica) – getting into the microbial environment, the sorbent acts like glue, enveloping microbial bodies and connect them into a single conglomerate.

Nanotechnology is science, engineering, and technology conducted at the nanoscale, which is about 1 to 100 nanometres.

NANO TECHNOLOGY

Aerosil R972 Pharma

However, the use of Silics is effective only for significant exudation. When the first granulation appears in a purulent wound, preparation cannot be prescribed due to excessive dehydration of healthy cells and the development of secondary necrosis. In order to reduce the osmotic activity of Silics, PHC added a hydrophobic sorbent - **Aerosil R972-Pharma**.

The role of Aerosil R972 in Pathelen® (in decreasing order of importance):

1. Decrease in too high hydrophilicity of A-300 in order to prevent over drying of the wound. The hydrophilicity of Pathelen can be regulated (Pathelen H, M, L) depending on the stage of the wound process.
2. Adsorption of hydrophobic pathogenic agents from wound exudation. These can be lipopolysaccharide toxins – products of metabolism and catabolism of wound microflora, fragments of cell membranes, some lipoproteins, polypeptides, etc.

3. Improving the technological properties of the powder – Pathelen® forms dust less than the A-300, has better flowability and does not stick to the walls of the bottle.

What the reason for the use of Benzalkonium Chloride ?

The surface of R972 is completely hydrophobic (covered with a continuous layer of methyl groups); therefore, the sorbent floats on the surface of the liquid like Styrofoam. But, for local use in a purulent wound, the medical device should be wetted by wound exudate.

Quaternary ammonium compounds, in particular Benzalkonium chloride, hydrophilize the surface of hydrophobic Aerosil, after which the suspension does not exfoliate, and the dried product is easily mixed with hydrophilic silicon dioxide in any ratio. A stable product is formed (triple composition), which is easily preserved for a long time (more than 3 years).

Thus, quaternary ammonium compounds are used as modifying intermediates between the hydrophobic and hydrophilic components of Pathelen. The composition of the medical device for the content of benzalkonium chloride is optimized based on the need for complete lyophilization of the surface of hydrophobic Aerosil.

That is why Nano composition Pathelen® consist of three components.

Identification

After intensive shaking, an air cushion forms between the nanoparticles and the medical device seems like “settle”, the particles roll on their walls (“ball bearing effect”), and when swaying, a pseudo-liquid consistency of the medical device is observed.

- «Ball bearing effect» – an air cushion forms and the medical device seems like “settle”;
- pseudo-liquid consistency of the medical device.

Mechano Chemical Immobilisation vs Mixing

The grinding of solid medical device is one of the main technological operations in the manufacture of medical device. In the process of machining solid mixtures in a ball mill, grinding and effective mixing of the components occurs. In this case, adsorption of one substance on the surface of another is also possible.

The hydrophobic Aerosil / benzalkonium chloride mixture was mechanically shaken in an atmosphere that contained 30% (by weight of Aerosil) of an ethanol solvent. The degree of coverage of the surface by benzalkonium chloride with the result reached approximately 95%. With an increase in the ethanol content in the atmosphere to 50% by weight of Aerosil and mechanical shaking of the mixture in a ball mill, **a complete surface coating is obtained.**

UNIQUE PROPERTIES OF PATHELEN®

The focus of the pathophysiology of sepsis is currently on the excessive inflammatory response of the body, not the pathogen itself. According to modern concepts, sepsis is not so much the presence of living bacteria in the patient's blood as the result of a "cascade" of reactions associated with the release of cytokines from macrophages stimulated by bacterial toxins.

PATHELEN® removes the WHOLE spectrum of toxic substances formed in a purulent wound, allowing to interrupt the development of SIRS and sepsis.

PATHELEN® neutralises and removes ALL microorganisms from the wound including multi-resistant, regardless of their type and resistance to antibiotics. The medical device does not have selective sorption, which avoids the selection of resistant strains.

- due to the nanoscale state, the particles of the medical device are adsorbed on the surface of microorganisms, causing their agglutination (like flour on meat).
- bacteria are easier to remove from the wound, because blocked their main centres of adhesion.
- production of exotoxins significantly decreases.

Animal studies have shown that the nanoparticles of the medical device are not absorbed into blood and do not accumulate in the internal organs after orally administration for 3-6 months.

BIOFILM

Medical Device of Choice

Biofilm formation involving *Staphylococcus aureus* may play a crucial role in the pathogenesis of chronic wound infection.

PHC investigated the effect of PATHELEN® on the biofilm formation ability of *Staphylococcus aureus* 8. (Research was conducted in the laboratory of Mechnikov Institute of Microbiology and Immunology, Kharkiv, Ukraine.)

It was found that after 48 hours of exposure there is a valid significant decrease in the biofilm formation ability from Medium to Low in strain of *Staphylococcus aureus* 8 compared with the daily culture.

It should be considered promising to study the clinical efficacy of PATHELEN® for local treatment of purulent wounds that do not heal for a long time and are associated with microbial biofilm formation.

Clinical practice better shows the results of scientific researches.

PATHELEN® has established itself as the “**medical device of choice**” for local treatment of putrefactive necrotic wounds, the healing of which has an unfavourable prognosis with mortality around 50%.

With anaerobic and putrefactive infections, deep protein breakdown occurs. Removal of microorganisms and their toxins, as well as the melting of necrotic tissues, are more effective in treating wound infections than an attempt to destroy microorganisms that have invaded the wound tissue using antibiotic therapy alone.

The use of PATHELEN® accelerates the cleansing of wounds from pus and necrotic tissue, contributes to the correction of SIRS and allows you to stop systemic antibiotic therapy much earlier.

BIOFILM

Medical Device of Choice

By accelerating the rejection and fusion of necrotic tissue, PATHELEN® removes an environment, conducive to the development of infection.

When using therapies that do not have a sorption effect, the terms for cleansing of wounds are significantly longer compared to PATHELEN®.

PATHELEN® is also the medical device of choice when saliva and lymph get into the wound after surgery for cancer of the larynx. The medical device blocks their corrosive effect, thereby preventing corrosion of the main vessels of the neck with the occurrence of profuse bleeding.

The patient underwent laryngectomy with radical neck dissection (Crile operation) for control of neck lymph node metastasis. On the 4th day after the operation, massive lymphorrhagia developed, which was complicated by suppuration of the wound and necrosis of skin flaps.

After 8 days of applying PATHELEN®, the wound cleared from purulent-necrotic contents, which made it possible to perform skin grafting.

In addition to local treatment of wounds of external localization, the medical device is used in the form of 1-3% suspension for washing deep cavities. The suspension is prepared ex tempore, the solvent is normal saline solution or an antiseptic, temperature like body temperature.

A homogeneous suspension is injected into the abscess cavity of the lung (Movie), brain, retroperitoneal space in pancreatic necrosis, for deep phlegmons of the neck and mediastinitis, intravesical with urine bladder infections, etc.

The cavity of gangrene of lung is evenly washed by the suspension when the body position is changed, turbid exudate is evacuated by drainage or through the draining bronchus when expectoration and coughing.



CONCLUSION

Thus, the obtained results allowed PHC, to classify wound sorption with PATHELEN® as one of the main means of debridement and detoxification of purulent wounds. Thanks to the use of PATHELEN® in a significant part of patients, it is possible to avoid prolonged loading with large doses of antibiotics. At the same time, the duration of the febrile period is reduced due to the activity of absorption of toxins from the wound. Laboratory markers of purulent-inflammatory diseases such as leucocytosis with neutrophilia, C-reactive protein, procalcitonin, cytokines (IL-1, IL-6, IL-8, IL-10, TNF- α) are normalised.

The effectiveness of the medical device is confirmed by the defence of 3 dissertations and is a fragment of two more in various fields of medicine: proctology, thoracic surgery, dentistry and maxillofacial surgery.

The medical device has been successfully tested in clinics of Ukraine, Italy, Nigeria and Ghana.

Pathelen Woundpowder and Pathelen Hybrid are the same product. Pathelen is sold under the Pathelen Wound Powder name in Ghana & Nigeria only.

CONTACT DETAILS



**DISTRIBUTING
MEDICAL INNOVATIONS
FOR WOUND CARE
PRODUCTS**

Licensee Agent Distributor Wholesaler

SVS House, Oliver Grove
London, SE20 7XJ, UK

www.unipharmagroup.com

info@unipharmagroup.com