Curtis Health Caps

Chlorheks PROTECT

Chlorheks Protect is a cosmetic product intended for hand sanitization, containing **chlorhexidine (0.3%) and phenoxyethanol (0.732%)**—substances with established anti-microbial activity—and excipients (Glycerin, PEG-6 Caprylic/Capric Glycerides, PEG-40 Hydrogenated Castor Oil, Ethylhexylglycerin, Chlorhexidine Digluconate, Parfum).

Chlorhexidine is an active anti-bacterial, anti-viral, and anti-fungal substance. Chlorhexidine contents in *Chlorheks Protect* lotion amount to 0.3%, while according to literature concentrations of above 0.12% exhibit anti-microbial effects. Moreover, phenoxyethanol contained in this product synergistically enhances the efficacy of chlorhexidine. Chlorhexidine shows advantageous persistent effects (residual activity) thanks to its ability to bind with proteins present in skin.

The *Chlorheks Protect* cosmetic product was tested in accordance with PN-EN ISO 17516:2014 for microbiological purity and meets the requirements for this class of products.

Pos.	Test type	Reference standard	UoM	Requirements*	Result
1.	Enumeration and detection of aerobic mesophilic bacteria	PN-EN ISO 21149:2017	CFU/g	≤2000	0
2.	Enumeration of yeast and mould	PN-EN ISO 16212:2017	CFU/g	≤2000	0
3.	Identification of *Escherichia coli*	PN-EN ISO 21150:2015	/1 g	absent	absent
4.	Identification of *Pseudomonas aeruginosa*	PN-EN ISO 22717:2015	/1 g	absent	absent
5.	Identification of *Staphylococcus aureus*	PN-EN ISO 22718:2018	/1 g	absent	absent
6.	Identification of *Candida albicans*	PN-EN ISO 18416:2015	/1 g	absent	absent

* Requirements of PN-EN ISO 17516:2014

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Chlorheks Protect also contains micelles, which help to gently and effectively remove the impurities accumulated on the hands. Such a specific formulation

of the product provides for adequate hygiene and simultaneous moisturising of the hands. Unlike alcohol-based products, *Chlorheks Protect* does not dry out the skin. *Chlorheks Protect* does not irritate the skin or cause allergies, which was confirmed in patch tests of the finished product.

All ingredients contained in *Chlorheks Protect* are approved for use in cosmetics in line with Regulation 1223/2009/EC and were used in appropriate concentrations. The presentation of the cosmetic product, and description of its effect were provided in the Safety Assessment file. The Safety Assessment for *Chlorheks Protect* and considerations of the state of the art confirmed that the product is safe and not harmful for human health under normal or foreseeable conditions of use when used in accordance with the instructions for use. This cosmetic product therefore meets all the requirements of Regulation 1223/2009/EC.

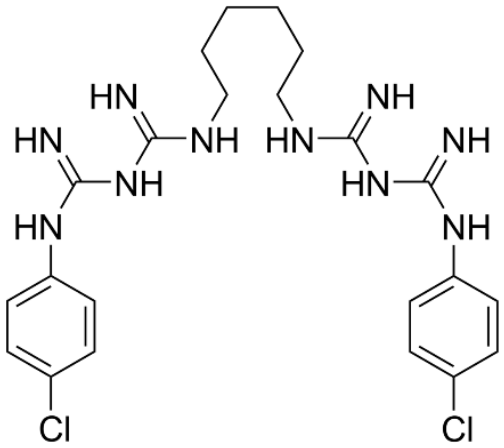
Advantages of using *Chlorheks Protect*:

- contains **anti-bacterial, anti-viral, and anti-fungal** agents,
- microbiological purity confirmed as per PN-EN ISO 17516:2014,
- exhibits prolonged activity,[1]
- it is safe, has topical effects only, does not absorb through skin,[1]
- it is gentle for hands, does not dry out the skin, does not irritate and sensitize (confirmed
  in the patch test),
- it has cleaning properties thanks to the presence of micelles,
- the product's composition is conforming to Regulation 1223/2009/EC on cosmetic products.

[1] Based on literature

Justification of effectiveness of Chlorheks Protect cosmetic product based on the analysis of literature data for the ingredients of the product, i.e., chlorhexidine and phenoxyethanol

Chlorhexidine



Structure

Chlorhexidine is a biguanide derivative used in a gluconated form (as chlorhexidine gluconate) in concentrations between 0.05% and 4% in numerous products, such as hand sanitizing washes, wipes, preoperative skin disinfection, vaginal antiseptic agents, or body washes for newborns, as well as in treatment of gingivitis (inflamed gums) and sepsis prevention [Weinstein *et al.*, 2008].

Mechanism of action

Chlorhexidine is a cationic molecule which non-specifically binds to negatively-charged phospholipid bacterial membranes, which results in membrane deformation and changes in the permeability of the bacterial cell wall to potassium and phosphorous ions. In low concentrations, chlorhexidine has bacteriostatic effect (i.e., inhibits development of bacteria), while higher concentrations (>0.12%) lead to further degradation of microbial cell wall and release of main intracellular components (including nucleotides), changes in microbial protein structure, coagulation of cytosolic proteins, which ultimately causes cell death by cytolysis [Karpiński and Szkaradkiewicz, 2015; Maillard, 2002; Tattawasart *et al.*, 2000].

Antimicrobial effects of chlorhexidine

Chlorhexidine exhibits:

- very good activity particularly against Gram-positive bacteria: *Streptococcus mutans* [MIC = 0.9–4 µg/mL], *Staphylococcus aureus* MSSA [MIC = 0.25–8 µg/mL], *Staphylococcus aureus* MRSA [MIC = 2–8 µg/mL], *Enetrococcus faecalis* [MIC = 4–16 µg/mL];
- good and moderate activity against Gram-negative bacteria: *Escherichia coli* [MIC = 2–16 µg/mL], *Klebsiela* spp. [MIC =8–16 µg/mL], *Pseudomonas aeruginosa* [MIC = 16–32 µg/mL];
- moderate and poor activity against fungi: *Candida albicans* [MIC = 1–16 µg/mL], *C. tropicalis* [MIC = 75 µg/mL], *C. krusei* [MIC = 150 µg/mL], *Aseprgillus* spp. [MIC = 8-64 µg/mL];
- minimal activity towards Mycobacteriaceae [Karpiński and Szkaradkiewicz, 2015; Emilson, 1977].

It is also active against enveloped viruses (predominantly in concentrations of 0.5%):

- herpes simplex virus type 1 (HSV-1), also in concentrations of 0.3%;
- influenza (flu) virus;
- human immunodeficiency virus (HIV);
- cytomegalovirus (CMV);
- respiratory syncytial virus (RSV) [Wood and Payne, 1998].

Chlorhexidine is almost **ineffective** against small non-enveloped viruses (rotaviruses, adenoviruses, enteroviruses, polioviruses, papillomaviruses) and it is not sporicidal [Karpiński and Szkaradkiewicz, 2015; Milstone *et al*., 2008].

The activity of the compound is practically unaffected in presence of organic substances (such as blood, saliva, and other bodily fluids) [Karpiński and Szkaradkiewicz, 2015].

Chlorhexidine, when used as a hand antiseptic, shows a beneficial affinity to proteins present on the skin surface—bound thereto, chlorhexidine in its active form is released over time, exhibiting **residual activity** and prolonged time of action [Weinstein *et al.*, 2008].

Safety of chlorhexidine

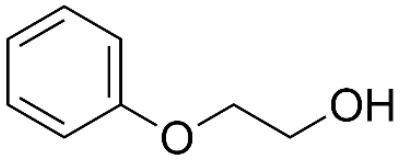
FDA considers chlorhexidine to be a **safe substance** which, however, may cause rare allergic reactions [FDA, 2017].

Chlorhexidine is virtually **not absorbed from the skin**. In in vitro human skin penetration studies, chlorhexidine penetrated the skin poorly after exposure for 2 and 30 minutes. In the upper layers of the skin (up to 100 µm), chlorhexidine concentrations amounted to 0.157 ± 0.047 and

0.077 ± 0.015 µg/mg of tissue, with minimal levels (less than 0.002 µg/mg of tissue) at deeper skin layers (below 300 µm) [Karpanen *et al.*, 2008].

Chlorhexidine, due to its safety and efficacy, is used broadly both in adults and children [Weinstein et al., 2008].

Phenoxyethanol



Structure

A phenylated derivative of ethylene glycol.

Used as a bacteriostat, commonly in a form of quaternary ammonium salt.

Enhanced bacteriostatic activity of combination of chlorhexidine and phenoxyethanol on *Escherichia coli* and *Pseudomonas aeruginosa* strains was confirmed in in vitro studies. It is believed that this effect is related to the increased outflow of potassium ions (K^+) and pentose from the bacterial cells in the presence of such combination [Fitzgerald *et al.*, 1992]. The efficacy of the combination was also confirmed against strains isolated in a clinical setting from 44 subjects with chronic periodontitis (inflammation of the tissues supporting the teeth). Chlorhexidine levels of 0.5 mg/mL inhibited the growth of bacteria cultured from all 44 samples, and comparable effects were obtained for phenoxyethanol levels of 20 mg/mL. However, the growth of bacteria from the samples was also inhibited by a combination of 0.125 mg/mL chlorhexidine and 5 mg/mL phenoxyethanol, i.e., at levels significantly smaller when compared to these agents used alone. Such combination has greater efficacy than each of these agents used alone. This study revealed that the addition of phenoxyethanol to chlorhexidine renders the combination an effective bactericide even at low concentrations [Wilson *et al.*, 1990].

Based on the literature review, the addition of wording stating the **anti-bacterial, anti-viral, and anti-fungal** activity is justified and supported by the data reported in the literature.

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