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Formulating a chlorhexidine based shampoo: a galenical challenge.

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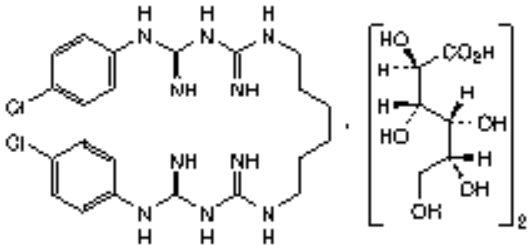
Chlorhexidine is an antiseptic agent of the biguanides group with an extensively documented bactericide and fungicide activity.

This molecule exists as various forms of salts: chlorhexidine diacetate, chlorhexidine dihydrochloride, or chlorhexidine digluconate, mainly differing by their solubilizing abilities in aqueous or oily media.

Chlorhexidine digluconate (or gluconate), as most soluble in water or alcohol, is the most used form in topical dermatology or cosmetic preparations.



Chlorhexidine digluconate

Chlorhexidine digluconate is a good antiseptic with a broad activity spectrum (Gram +: Staphylococci and Gram -: Pseudomonas), and an antifungal action for a 3% concentration.
Its antibacterial and antifungal characteristics are used in proprietary medicines for human and veterinary uses.

However, due to its chemical structure and cationic characteristic, chlorhexidine digluconate has many incompatibilities that make a simple formulation, like shampoo, a true galenical challenge. Moreover, high concentration incorporation makes the formulation even more difficult.

To formulate this active substance, many parameters need controlling:

- excipients, avoiding in particular any anionic compound especially anionic surfactants commonly used in shampoo formulations (due to their high foaming potential).
  Indeed, when in presence of anionic compounds, chlorhexidine digluconate has a tendency to form insoluble complexes. Likewise, although clear physical signs of incompatibility are not always detectable, products such as soaps, alginates, carboxymethyl cellulose or glycerin tend to reduce the biological activity of chlorhexidine by complexation.
- PH —between 5.5 and 7— for optimum efficacy of the molecule.
- manufacturing process, equipment and environment to avoid any "contamination" of the product during production that could alter its activity.

Physical and chemical stability and the activity of the formulation must be assessed individually.

One must also note that an evolution of the molecule's chemical form (due to interaction with another compound of the formula leading to its complexation) could modify its activity, and may not be necessarily correlated to a **detectable** chemical instability. Indeed, classical analytical techniques, used routinely, do not necessary reveal a complex form of chlorhexidine digluconate

in the speciality. It is therefore necessary at every step of production to check its activity with *in vitro* antibacterial and antifungal activity tests on sensitive and target germs (namely *Staphylococcus intermedius*, *Pseudomonas aeruginosa* and *Malassezia pachydermatis*).

To clarify this, a recent study compared the *in vitro* antimicrobial activity of various marketed shampoos with 2 to 4% Chlorhexidine digluconate, and revealed that optimum efficacy is not necessarily achieved for the formulation with the highest percentage of chlorhexidine (D.H. Lloyd , A.I. Lamport. Activity of chlorhexidine shampoos *in vitro* against *Staphylococcus intermedius*, *Pseudomonas aeruginosa* and *Malassezia pachydermatis*. *Veterinary Record*. 1999 ; **144**: 536-537).

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