

FeF[®] Quats in ophthalmics

Description

Multidose pharmaceutical products are prone to contamination, both from environmental and corporeal flora. Microbial contamination can present a threat to the safety, the purity or the efficacy of ophthalmic products, hence the importance of utilizing an effective preservative. For formulations coming into contact with corneal tissue, it is necessary to preserve against contamination by utilizing only the purest and safest ingredients. In both human and veterinary ophthalmics, one of the most common and effective preservatives is Benzalkonium Chloride (BKC / BAK).

Our FeF[®] Benzalkonium Chloride is widely used as an excipient in ophthalmic solutions, gels and ointments, where its concentration typically varies from 0.001% up to 0.01%.

Properties

The different alkyl (fatty) chain lengths give Quats different properties. For example, antimicrobial activity is greater for shorter chain lengths, however skin sensitivity decreases as the chain length increases. Shorter chain lengths are more soluble, and they also foam more.

The alkyl chain length distribution often plays a major role for ophthalmic formulators. Our production and process know-how allows us to offer Quats with a completely well-defined alkyl chain length distribution, whether it is with our standard chain length or with customized chain length distributions. Our standard chain length distribution in Benzalkonium Chloride is approx. 65% C12 and 35% C14, with max. 5% of C16. We also offer other chain length distribution products or can develop your own, customized product.

Alkyl chain length

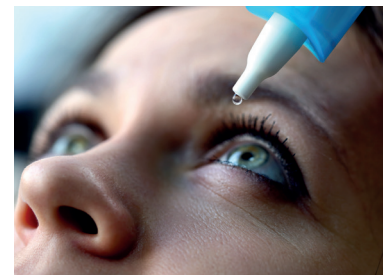


Product characteristics

Solubility: FeF[®] Quats are miscible with water or lower alcohols, such as methanol, ethanol and propanol in all ratios. They are not miscible with benzene or ether. Indicative solubility of Quats in %w/w at 20°C in water:

Tertiary Amine Carbon Chain Length (Alkyl Chain Length)	Benzyl chloride – Mix to form BKC
C12	70
C14	10
C16	1.5
C18	0.5

Solubility decreases as the alkyl chain length increases.



Compatibility: Mixing BKC with ordinary soaps and/or with anionic detergents may decrease the activity. As Quats are cationic compounds, they should not be mixed with anionic compounds which would have a neutralizing effect. Quats can be inhibited by Tween® and by lecithin.

Avoid mixing Benzalkonium Chloride (BKC) with citrates, iodides, nitrates, permanganates, salicylates, silver salts and tartrates. Incompatibilities have also been reported with other substances including aluminium, fluorescein sodium, hydrogen peroxide, kaolin and some sulfonamides. Hyaluronic acid can minimize BKC's irritating effect.

Stability: 5 years shelf life.

Other: Odourless, Colourless, Easy to formulate, Surface active / adhesive, Non-volatile and very stable.

Antimicrobial effect

FeF® Quats are effective at all pH levels. However their effectiveness increases when the pH increases. The higher the pH, the lower the concentration needed to obtain an antimicrobial effect. As opposed to bacteriostatic/fungistatic compounds which only prevent micro-organisms from dividing (growing), Quats are bactericidal/fungicidal meaning they will kill micro-organisms whether they are in a growth phase or not.

FeF® BKC has been tested against several relevant microbial strains, and shown to be effective against a wide range of microorganisms at low concentrations. FeF® BKC is compared here with ethanol and with a positive control containing Meropenem (a broad-spectrum antibiotic). See Table 1.

Table 1: Minimal Inhibitory Concentrations. Mean results in % or µg/ml.

Species	ATCC no.	BKC %	Ethanol %	Meropenem µg/ml	Control strain/ Meropenem µg/ml	Range of control µg/ml
Candida albicans	2091	< 0.001	>1	>16	-	-
Corynebacteria amycolatum	CCUG 33685	0.002	>1	0.006	0.06-0.25	0.06-0.25
Streptococcus dysgalactiae	12394	< 0.001	>1	< 0.015	0.06-0.25	0.06-0.25
Enterococcus faecalis	29212	< 0.001	>1	0.125-8	-	-
Staphylococcus aureus MRSA	33591	< 0.001	>1	16	2-8	2-8
Staphylococcus aureus	29213	< 0.001	>1	0.06	-	-
Pseudomonas aeruginosa	27853	0.008	>1	0.5	0.03-0.12	0.03-0.12
Mycobacterium abscessus NFM32	-	< 0.001	>1	< 0.001	0.25-1	0.25-1
Acinetobacter baumannii	19606	0.002	>1	1	-	-
Staphylococcus epidermidis	12228	< 0.001	>1	0.06	-	-
Staphylococcus lugdunensis	70328	< 0.001	>1	0.25	-	-

Statens Serum Institute, Denmark (2016)