



HALAMID®

BIOCIDAL MODE OF ACTION

Historical view on the biocidal mode of action

Since the first publication by Chattaway(1) in 1905 on Chloramine T and the first introduction as a disinfectant by Dakin(2) in 1916, this product has been seen as slow hypochlorite (HOCl and/or OCl⁻) releasing agent. This despite some authors reported about properties conflicting with this theory(3,4).

Product properties conflicting with the theory of slow hypochlorite release in comparison to hypochlorite and chloro-isocyanurates are:

- excellent stability of the aqueous solution
- moderate pH dependence of the biocidal efficacy
- moderate influence of organic matter on the biocidal efficacy
- hardly any skin irritation
- hardly any chlorination ability

New Studies I

Recently some studies have been published that prove that the biocidal mode of action of Halamid® is not based on the release of hypochlorite but must be explained by a different chemical mechanism.

Gottardi(5) calculated the theoretical composition of an aqueous Chloramine-T solution at various pH values. In an aqueous solution of Chloramine-T the following equilibriums exist: (R= CH₃-C₆H₄-SO₂)



According to these equilibriums, seven different compounds can be present in a Chloramine-T solution.

Based on the known equilibrium constants, Gottardi calculated for various pH values the concentrations of the individual compounds. If Chloramine-T would be a slow hypochlorite-releasing agent, then the compounds HOCl and/or OCl⁻ should be present at a significant level. However Gottardi showed that for a 0.1 % Chloramine-T solution the hypochlorite concentrations [OCl⁻] and [HOCl] are:

at pH 3 : [OCl⁻] = < 0.01 µg/l, [HOCl] = 14 µg/l
 at pH 7 : [OCl⁻] = 4 µg/l, [HOCl] = 14 µg/l
 at pH 10 : [OCl⁻] = 35 µg/l, [HOCl] = 0.5 µg/l
 at pH 12 : [OCl⁻] = 200 µg/l, [HOCl] = < 0.01 µg/l

The biocidal effects of Chloramine-T can never be explained by these minimal quantities of hypochlorite.

New Studies II

Hahn et al(6) proved the theory of Gottardi by analysis. They developed an electrochemical analytical method by which they could detect very low concentrations of hypochlorite in a Chloramine-T solution. They found that in an aqueous solution containing 2.5 g Chloramine-T per liter, the hypochlorite concentration is lower than 100 µg/L (this is the detection limit of the analytical method). Even if they deliberately add hypochlorite to the solution, it reacts quickly with solution components. At neutral and alkaline pH values, it reacts with R-NH₂ (para-toluenesulfonamide), which -as Gottardi shows- is present at minor concentrations in a Chloramine-T solution, to form Chloramine-T. At acidic pH values it is reported to react with R-NHCl to form RNCl₂ (dichloramine-T).

So based on theoretical as well as analytical proven facts one has to conclude that Halamid® is not a slow hypochlorite releasing agent.

Present view on the biocidal mode of action of Halamid®

Gottardi calculated that the compounds responsible for the biocidal properties of a Chloramine-T solution are:

- at pH < 3: R-NHCl and R-NCl₂ (Chloramine-T acid and Dichloramine-T)
- at pH 3 to 6: R-NHCl, R-NCl⁺ and R-NCl₂ (Chloramine-T acid; Chloramine-T ion and Dichloramine-T)
- at pH > 7: R-NCl⁺ (Chloramine-T ion)

At all pH values, these molecules represent more than 99.99 % of the total amount of Chloramine-T present in the solution.

Biocidal mode of action of Halamid®

Halamid®, dissolved in water, ionizes and forms the Chloramine-T ion. This ion reacts directly with microorganisms such as bacteria, fungi, viruses, with which it comes into contact. Its action is based on an irreversible destruction of the envelope and cell material of microorganisms. This oxidizing action ensures that microorganisms are effectively killed and do not have a chance to develop resistance to Halamid®.

References:

- 1 F.D. Chattaway, J. Chem. Soc. 87, 151 (1905)
- 2 H.D Dakin, J.B. Cohen, M. Daufresne, J. Kenyon, Proc. Royal Soc. London Ser. B. 232-251, 1916
- 3 Kirk-Othmer, Encyclopedia of Chemical Technology, 5th edition, Volume 5, page 921
- 4 Ullmann's Encyclopedia of Industrial Chemistry, 4th edition, Band 9, page 389
- 5 W. Gottardi, Arch. Pharm., 325, 377-384, (1992)
- 6 M. Hahn, A. Liebau, H.H. Rüttinger, R. Thamm, Anal. Chim. Acta, 289, 35-42, (1994)

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HALAMID®

LISTING OF SPECIES TESTED

Halamid® has proven effective against all types of microorganisms (Gram positive and Gram negative bacteria, naked and enveloped viruses, fungi and parasites) ensuring a reliable result where disinfection is vital.

Check the list of microorganisms against which Halamid® is effective to discover its large active spectrum.

The applied concentration and contact time required are the critical parameters thus contact us for more details on a specific microorganism for your application.

Bacteria

Achromobacter anitratus
 Acinetobacter spp
 Actinobacillus pleuropneumoniae
 Aeromonas hydrophila
 Aeromonas salmonicida
 Agrobacterium tumefaciens
 Alcaligenes faecalis
 Bacillus anthracis
 Bacillus cereus
 Bacillus diptheria
 Bacillus dysentery
 Bacillus flavothermus
 Bacillus mesentericus
 Bacillus subtilis spores
 Bacillus subtilis
 Bacillus thuringiensis
 Bacterium enteritidis Gaertner
 Bacterium paratyphi
 Bacterium rhusopatha
 Bacterium septamicariae haermorigicael
 Bacterium typhi gallinarum
 Brachyspira intermedia
 Brachyspira pilosicoli
 Brucella abortus bang
 Brucella suis
 Campylobacter spp. Jejuni
 Carnobacterium piscicola
 Citrobacter spp.
 Clavibacter michiganese
 Clostridium welchii
 Clostridium sporogenes
 Clostridium bifermentas
 Clostridium tertium
 Clostridium histolyticum
 Clostridium caloritolerans
 Corynebacteriummichiganese
 Corynebacterium spp.
 Enterobacter aerogenes
 Enterobacter cloacae
 Enterobacteriaceae Citrobacter

Enterobacteriaceae Hafnia
 Enterobacteriaceae Klebsiella
 Enterobacteriaceae Kluvera
 Enterobacteriaceae Serratia
 Enterococcus faecium
 Erwinia carotovora
 Escherichia coli
 Escherichia tarda
 Flavobacterium branchiophilum
 Flavobacterium columnaris
 Flavobacterium haematocrits
 Flexibacter maritimus
 Geotrichum candidum
 Isaria farinose
 Klebsiella oxytoca
 Klebsiella pneumoniae
 Lactonacillus spp.
 Lawsonia intracellularis
 Legionella pneumophila
 Listeria monocytogenes
 Micrococcus avium
 Micrococcus citreus
 Micrococcus pyogenes
 Moraxella spp
 Mycobacterium avium
 Mycobacterium lacticola
 Mycobacterium minetti
 Mycobacterium pellegrino
 Mycobacterium phlei
 Mycobacterium piscium
 Mycobacterium smegmatis
 Mycobacterium vole bacillus
 Pasteurella
 Pediococcus cerevisiae
 Proteus mirabilis
 Proteus vulgaris
 Providencia alcalifaciens
 Pseudomonas aeruginosa
 Pseudomonas fluorescens
 Pseudomonas fragi
 Pseudomonas putida
 Pseudomonas putrefaciens
 Pseudomonas pyocyanea
 Pseudomonas solanacearum

Pseudomonas tolaasii
 Pyocyaneus
 Salmonella anatum
 Salmonella dublin
 Salmonella durban
 Salmonella livingstone
 Salmonella newbrunswick
 Salmonella newport
 Salmonella oranienburg
 Salmonella paratyphi B
 Salmonella pullorum
 Salmonella rostock
 Salmonella senftenberg
 Salmonella thompson
 Salmonella typhimurium
 Sarcina lutea
 Serratia marcescens
 Serratia liquefaciens
 Shigella boydii
 Shigella sonnei
 Spicaria pracina
 Staphylococcus aureus
 Staphylococcus aureus haemolyticus
 Staphylococcus bag
 Staphylococcus epidermidis
 Staphylococ. paratyphosa B
 Staphylococcus pyogenes
 Streptococcus agalactiae
 Streptococcus faecalis
 Streptococcus faecium
 Streptococcus lactis Blaser Sveitsi
 Streptococcus suis
 Tail rot disease
 Vibrio alginoliticus
 Vibrio anguillarum
 Vibrio cholerae
 Vibrio harveyi
 Vibrio parahaemolyticus
 Vibrio salmonicida
 Vibrio vulnifious
 Yersinia enterocolitica
 Yersinia pseudo-tuberculosis
 Yersinia ruckerii
 Xanthomonas hyacinthi

Viruses

Adenovirus
African swine fever virus
Aujeszky Disease virus
Avian influenza A virus
Avian reovirus
Canine parvovirus
Celovirus
Classical swine fever virus
Corona virus
Coxsackie virus
Diphtheria virus
Ektromelie virus
Encephalomyocarditis virus
Enteric cytop. bovine orphan virus (ECBO)
European swine fever virus
Foot and Mouth Disease virus
Fowl plague virus
Fowl pox virus
Gumboro Disease virus
Hepatitis A virus
Hepatitis B virus
Hepatitis contagiosa canine virus
Herpes virus
Human Immuno-Deficiency virus (HIV)
Human rotavirus
Infectious bronchitis virus
Infectious bursitis virus
Infectious pancreatic necrosis
Infectious salmon anaemia (ISA) virus
Influenza virus
Irido virus (ASFV)
Myxomatosis virus
New Castle Disease virus (NCD)
Nuclear polyhedron virus
Orthopox commune virus (vaccinia)
Parainfluenza virus
Paramyxo virus
Picorna virus
Poliovirus
Porcine parvovirus
Pox virus
Pseudo Bird Pest virus
Rabies virus (fixed)
Reovirus
Retro virus
Rhino pneumonic virus
South African Pest virus
Swine fever virus
Systematic ectodermal and mesodermal
baculo virus (SEMBV)
Teschen virus
Toga virus
Vaccinia virus
Vesicular Swine Disease virus
White spot disease virus (SMBV)

Fungi

Aspergillus amstellodami
Aspergillus flavus
Aspergillus fumigatus
Aspergillus gr. glaucus
Aspergillus niger
Aspergillus oryzae
Aspergillus ochraceus
Aspergillus versicolor
Byssochlamys nivea
Chaetomium globosum
Cladosporium herbarum
Cladosporium cladosporoides
Entomophthora destruens
Entomophthora thaxteriana
Entomophthora virulenta
Epidermophyton floccosum
Fusarium moniliforme
Geotrichum candidum
Microsporum canis
Microsporum gypseum
Myrothecium verrucaria
Oöspora lactis
Paecilomyces variotii
Penicillium cyclopium
Penicillium funiculosum
Penicillium granulatum
Penicillium roqueforti
Penicillium verrucosum
Saprolegnia parasitica
Tilletia caries
Trichoderma viride
Trichophyton equinum
Trichophyton mentagrophytes
Walleimia ichthyophaga

Algae

Chlorella vulgaris
Skeletonema sp.
Tetraselmis sp.

Yeasts

Candida albicans
Cryptococcus spp
Saccharomyces cerevisiae
Saccharomyces diastaticus

Parasites

Epistylis
Gill trematoda
Gyrodactylus salaris
Ichtyobodo necator
Ichthyophthirius multifiliis
Labyrinthuloides haliotides (Labyrinthomorpha)
Neoparamoeba pemaquidensis

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HALAMID® IN FORMULATIONS

For most applications, Halamid® is simply dissolved in water and used as such with excellent results. In some peculiar situations, it can however be interesting to formulate Halamid®. Such applications include for example laundry and dish washing detergents, kitchen and lavatory cleaners, cow-teat disinfectants, where Halamid® is used either for its properties as a disinfectant or as an oxidizing agent. Because of its excellent stability together with the wide range of compatible products, Halamid® is an excellent product to be used in liquid or solid formulations.

Compounds to avoid

Halamid® being an oxidizing compound, reducing compounds should not be mixed with it, to avoid inactivation. Compounds containing amine or ammonium groups should also be avoided as exchange of the active chlorine might occur with Halamid®.

Acidic compounds (or compounds forming acidic compounds by oxidation) cannot be used in Halamid® formulations: they induce a decomposition of Halamid® over time, thus reducing stability and shelf life of the formulation (cf below pH control).

Surfactants

Halamid® itself does not have any surface tension activity, but it can perfectly be used in combination with non-ionic surfactants (eg ethoxylated fatty acids and ethoxylated nonylphenols), or anionic surfactants (such as alkylsulphonates or alkylsulfates).

Viscosity

To increase the viscosity of liquid Halamid® solutions, carboxymethyl cellulose, polyvinyl alcohol and polyacrylates can be added.

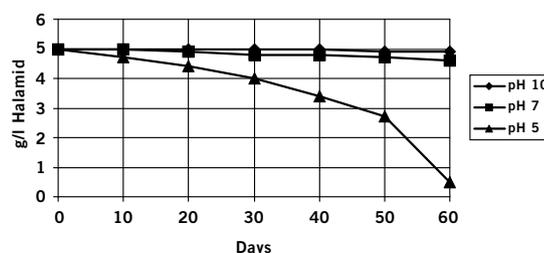
Chelating agents

Chelating agents such as polyphosphates, aminopolycarboxylates and phosphonic acid based chelates can be used in Halamid® formulations to reduce the influence on properties of water hardness (calcium and magnesium ions) and presence of other trace metals.

pH control

When dissolving Halamid® into water, a neutral to weakly alkaline solution is obtained, depending on the concentration. Acidic pH has a negative effect on Halamid® stability as shown on the graph below, but additives to increase the pH / buffer Halamid® formulations can easily be used. Such compounds include sodium and potassium carbonates, metasilicates, sodium and potassium hydroxide.

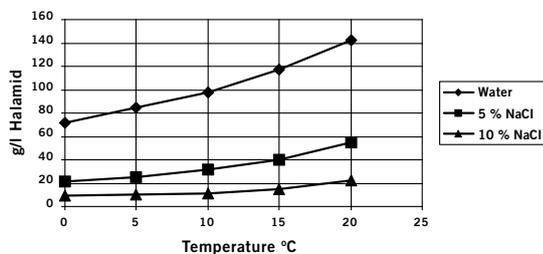
Stability of Halamid® solutions at various pH



Solubility

For liquid formulations it is important to avoid crystallization. The graph below shows the solubility of Halamid® in water at different temperatures as well as the influence of salt content of this parameter.

Solubility of Halamid® in water at various temperature and salt content



Influence of light

Halamid® stability is negatively influence by light, therefore an opaque container is required to ensure Halamid® formulations are stable over time.

Examples of liquid and solid formulations containing Halamid® are available in the literature and can be obtained on request.

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CORROSION DATA

NOT CORROSIVE TO EQUIPMENT, HOUSING, ETC.

According to EC-regulations Halamid® is to be labeled as a corrosive substance. However, this classification is based on the result of a skin irritation test performed with Halamid® as a moistened solid powder. These tests have no relevance for determining material corrosion.

When applied as a disinfectant, Halamid® is always used in an aqueous solution. The results of material corrosion tests with a 0.5% Halamid® solution tests are presented in the table on the reverse side of this bulletin. From the results it can be concluded that Halamid® has no or only a minor corrosive effect on materials commonly used in farms, shops, institutes and industries, like stainless steel, aluminum, concrete, wood, polymers.

HALAMID®, A UNIQUE PRODUCT

- Large activity spectrum
- Non corrosive in solution for materials
- Easy to use and versatile
- Stable
- Readily biodegradable
- No risk of building up resistant microorganisms

Corrosion table of Halamid® solution (0.5% in water)

Objects exposed to continuous agitation at 50°C for 48 hrs.

Material	Weight g/m ² /day	Description of the object	Description of solution after treatment	Judgment
Nickel free Chromic Steel	- 0.66	light corrosion on the welding seam	practically unchanged, clear	practically fully resistant
Iron	58.92	etched	clear, colourless, dark brown deposit	not very good resistant
Iron, tinned	- 0.48	build-up of a mat-layer with good adhesion	practically unchanged, clear	practically fully resistant
Brass	0.11	practically unchanged	practically unchanged, clear	practically fully resistant
Copper	- 3.58	not attack. build-up of a rough layer with good adhesion	practically unchanged, clear	practically fully resistant
Alu-composition	0.16	darkly coloured with many white spots	practically unchanged, clear	practically fully resistant
Pure aluminum	- 0.80	darkly coloured	practically unchanged, clear	practically fully resistant
Wood-teak	- -	whitened slightly more porous surface	light yellow	resistant
Oak	- -	some yellowing	light yellow	resistant
Mahogany	- -	some yellowing	light yellow	resistant
Rubber	- -	some yellowing	light yellow	fully resistant
Plastics (PE-PVC etc.)	- -	unchanged	unchanged	fully resistant

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HALAMID® - STABILITY DATA

Halamid® is a universal, effective, readily biodegradable disinfectant with superior storage stability. Tests have shown that Halamid® is a very stable product, both as a powder and as a solution, ensuring that it remains ready for use with full efficacy whenever you need it.

Halamid® has a shelf life of two years after production date when stored in the closed original packaging, in a cool and dry place, away from direct sun light and heat.

Storage stability

Tests have shown that, if properly stored, Halamid® will not undergo significant changes in quality even after several years of storage.

In order to determine the storage stability of Halamid® under tropical conditions a test was performed at 35°C and 85% relative humidity.

25 kg of Halamid® packed in its original 4 ply paper bag were placed in a constant climate cupboard for 120 days. During this period the weight and the content of the Halamid® were regularly checked. After 120 days of storage at 35°C and 85% relative humidity the Halamid® packed in its original bag proved not to have been changed in weight or content.

A similar test was run with Halamid® in open contact with the humid air.

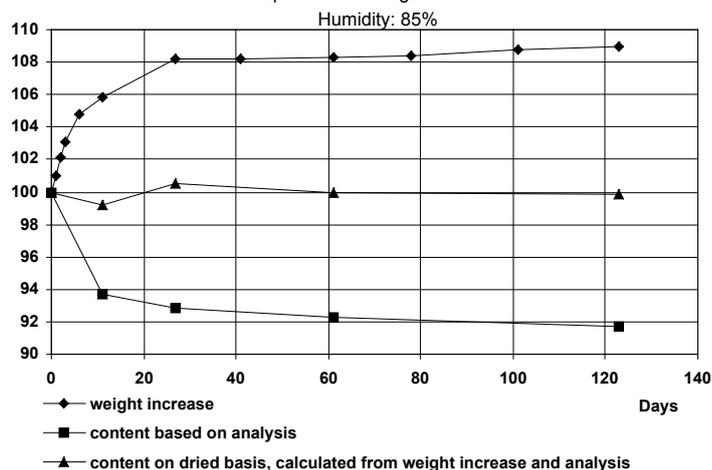
In the first 30 days of this experiment the weight of the Halamid® increased while the content declined. After that period the weight and content of the Halamid® were more or less stable.

The weight increase was caused by water adsorption, which resulted in a content reduction exactly proportional to the content decrease analyzed. No decomposition of Halamid® could be detected.

All this proves that Halamid® is a product with superior storage stability even under non-ideal conditions.

Halamid® Stability under Tropical Conditions

Test condition: direct contact between Halamid and air
Temperature: 35 degrees Celsius



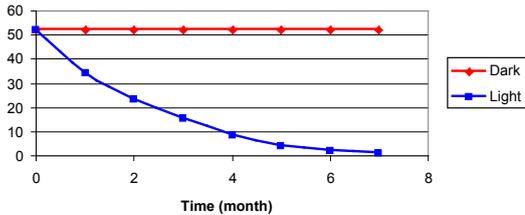
STABILITY IN SOLUTION

The available data show that Halamid® solutions prepared with clean water and store away from light and heat are very stable, which makes possible to prepare stock solutions.

Influence of light

From the graph below, it is clear that a Halamid® solution stored in the dark (using an opaque container) can be stored for several months without decomposition.

Influence of light, 5% Halamid® solution

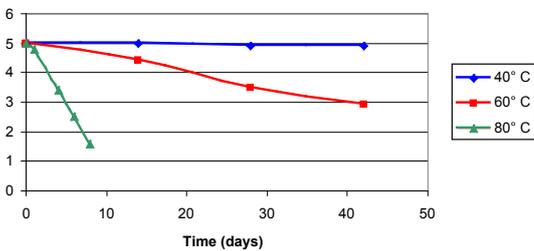


It is important to avoid exposure of Halamid® solutions to sunlight if they are to be kept for a certain period of time.

Influence of temperature

Even at elevated temperature, Halamid® solutions show good stability. For example, after 4 weeks at 40°C, only 2% of activity is lost.

Influence of temperature, 0.5% Halamid® solution

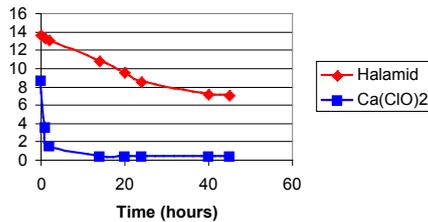


Influence of organic matter

Presence of organic matter has only a limited effect on Halamid® efficacy. It is for example recognized that Halamid® is much less affected by organic matter than hypochlorite.

To illustrate this, Halamid® and hypochlorite solutions were prepared using river water. After only a couple of hours, the vast majority of hypochlorite is degraded by reaction with the organic matter present, while after 2 days, there are still about 50% of the original Halamid® concentration available.

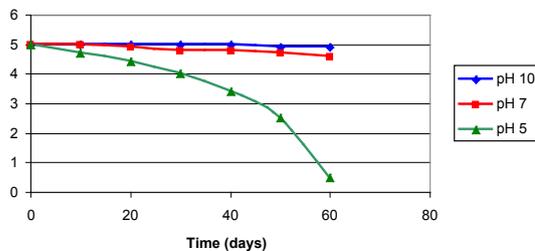
Halamid® vs hypochlorite (river water)



Influence of pH

The graph below show the influence of pH on stability of a Halamid® solution. Under neutral / alkaline pH condition, the Halamid® solution is very stable. Under acidic conditions, Halamid® is degraded, one of the reasons why acidic compounds should not be mixed with Halamid® in formulations.

Influence of pH, 0.5% Halamid® solution



All the available data point to the stability of Halamid®, both as a solid as well as in solution

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