

Enhancement of Solubility and Activity of Triclosan by Entrapment in Polysaccharide Delivery Systems

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Introduction

Triclosan is a potent antimicrobial agent with a wide activity spectrum against both gram positive and gram negative bacteria, and against yeast and moulds. It is thus widely used in personal care products such as toothpastes, shampoos, shower gels, and deodorants, in beauty products and as in anti-acne treatments. However, its insolubility in water makes its formulation difficult.

Triclosan has been entrapped in two delivery systems, both based on meshed polysaccharides which are water dispersible, in order to improve its incorporation into formulas. Its antimicrobial activity has then been tested.

Objective

Triclosan in solution, or entrapped in either Glycospheres or Softspheres was tested in order to determine the capacity of the two polysaccharide delivery systems to enhance its antimicrobial activity.

Sample Preparation

First experiment :

- TC : Solution of triclosan in Butylene Glycol / Water (10 / 90).
- Gs-TC - Entrapped triclosan in Glycospheres : a suspension of Gs-TCB containing 1% (w/w) triclosan is diluted in Butylene Glycol / Water (10 / 90)
- Sp-TC - Entrapped triclosan in Softspheres : 1 gram of Softspheres Sp-TC16a containing triclosan (3% w/w) is broken and dispersed in a solution of Butylene Glycol / Water (10 / 90) to form a suspension.

All samples contain the same amount of triclosan (0.1%) and of Butylene Glycol (10%).

Second experiment :

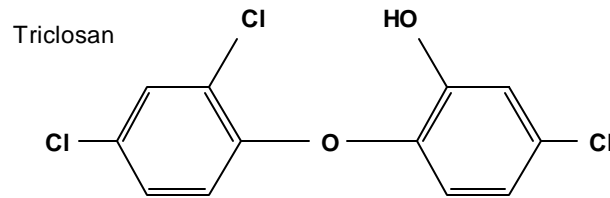
- TC : Solution of triclosan in Butylene Glycol / Water (90 / 10).
- Gs-TC - Entrapped triclosan in Glycospheres : a suspension of Gs-TCB containing 1% (w/w) triclosan is diluted in Butylene Glycol / Water (90 / 10)
- Sp-TC - Entrapped triclosan in Softspheres : 1 gram of Softspheres Sp-TC16a containing triclosan (3% w/w) is broken and dispersed in a solution of Butylene Glycol / Water (90 / 10) to form a suspension.

All samples contain the same amount of triclosan (0.1%) and of Butylene Glycol (90%).

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Triclosan

Triclosan is a broad-spectrum antimicrobial agent approved for use in toothpastes and in toiletry products. It also has anti-irritant /anti-inflammatory properties. It is soluble in most organic solvents, but only sparingly soluble in water and needs to be either dispersed with the aid of surfactants or solubilized in solvents, thus limiting its usage.

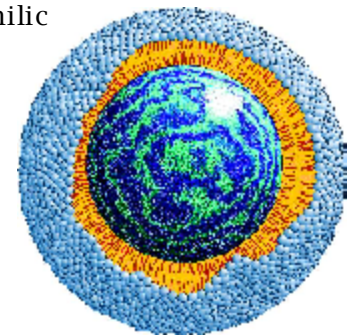


Glycospheres

Glycospheres are supramolecular systems, organized around a stable inner core, having an average diameter of 200 nanometers. They are composed of three compartments (from the inside to the outside) :

- An inner matrix made of quaternarized and cross-linked starch : in this compartment, anionic and hydrophilic ingredients can be entrapped by means of ionic bonds and be protected and delivered;
- A layer of fatty acids, covalently bonded to the periphery of the starch matrix by ester bonds, giving the system a capacity to load lipophilic compounds;
- An outer layer(s) of lecithins, which gives to Glycospheres its ability to disperse in water or in other polar solvents.

Numerous studies have shown the capacity of Glycospheres to entrap active molecules, to protect them from degradation and to potentialize their activity.



Softspheres

Softspheres are large (0.5 to 3 millimeters) spheres, made of agar-agar, a natural polysaccharide. A cationic and amphiphilic copolymer is also embedded within the agar matrix, giving to the system a capacity to trap active molecules by means of ionic bonding or hydrophobic interaction. They can also be colored and used for decoration of transparent cosmetic preparations.

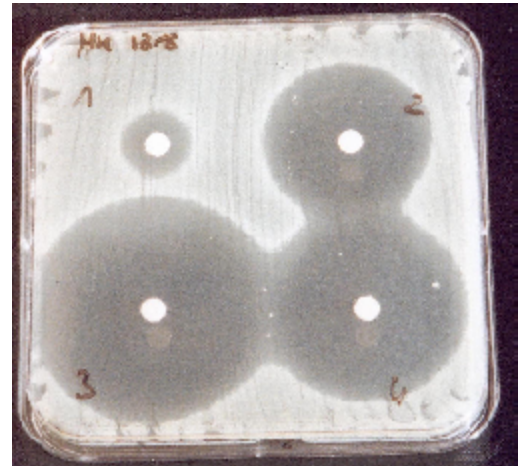


1. Study of the bactericidal activity of triclosan

20 microliters of each solution were deposited on a paper disk. The disks were then placed at the surface of an agar media containing *Staphylococcus aureus* (ATCC 53154). After 24 hours at 37°C, inhibition diameters are measured. Percentages of increase in activity were calculated as follows :

$$\% \text{ increase} = \frac{(\text{Gs-TC} - \text{Solv}) - (\text{TC} - \text{Solv})}{(\text{TC} - \text{Solv})}$$

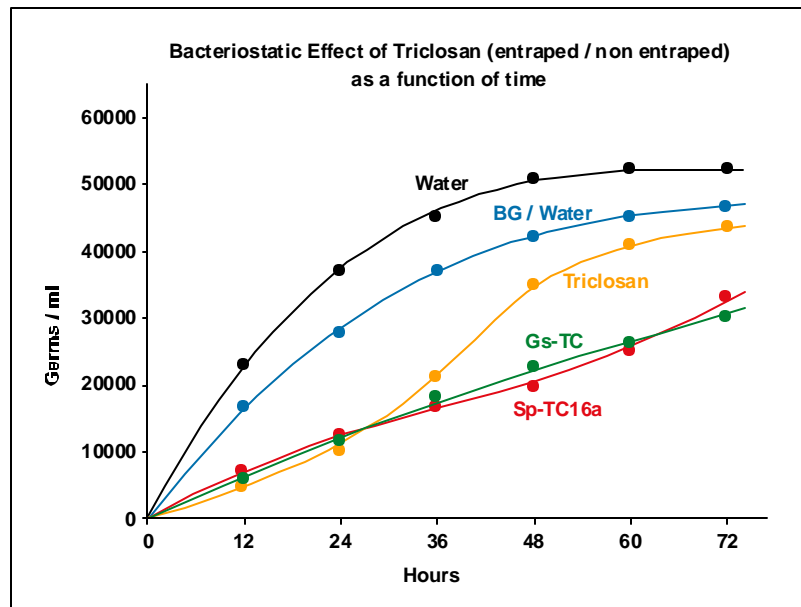
Sample	Content	Inhibition Diameter (mm)	Activity Increase (%)
Solvent	Butylene Glycol / Water (10 / 90)	19	-
TC	Triclosan in solvent	44	-
Gs-TC	Triclosan entrapped in Glycosphere	64	80%
Sp-TC	Triclosan entrapped in Softsphere	52	32%



The results show that both Gs-TC and Sp-TC exhibit a much higher capacity to inhibit the growth of *S. aureus*.

2. Study of the bacteriostatic activity of triclosan

1 milliliter of each sample (preparation method #2) and 9 milliliter of Tryptone-salt media are mixed in a test tube for a final concentration of 0.1% triclosan. Each test tube is kept at 37°C. Every 12 hours, 1 milliliter of each solution is added to a Petri dish; a Trypticase soy medium is then poured and incubated at 37°C during 48 hours for bacterial numeration.



The results show that triclosan in solution is only active, in these conditions, for a short period of time : after 36 hours, the protection of triclosan is very limited. On the contrary, Gs-TC and Sp-TC both show a higher bacteriostatic activity than non entrapped triclosan (TC), even after 72 hours. The activity of both delivery systems seems in this experiment very similar.

Conclusion

In this study, we have shown that triclosan can be entrapped in two different types of polysaccharide delivery systems : glycospheres and softspheres.

The bacteriostatic activity of triclosan, either in solution or in an entrapped form, has been demonstrated on *Staphylococcus aureus*.

When entrapped, triclosan exhibits a much higher (up to 80%) activity as compared with the non-entrapped form.

Entrapped forms of triclosan also have a longer lasting activity (more than 72 hours).

Work is now in progress in order to show similar pattern on other models, either bacteria or yeast.

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