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Professor Ivan Draganić

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SYNTHESIS OF GUM ARABIC-NATAMYCIN CONJUGATE

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Abstract

In this work, natamycin, a polyene antibiotic belonging to the family of macrolides, was coupled to the periodate oxidized polysaccharide gum Arabic. Resulting conjugate was characterized by UV-Vis and FT-IR data.

Introduction

Natamycin (pimaricin) is a polyene macrolide antibiotic produced during fermentation by *Streptomyces natalensis*. This antibiotic (Fig.1.) Has been used for many years in the food industry as well as in veterinary medicine, but insolubility in water limits its wider use. Gum Arabic is a water soluble, highly branched complex polysaccharide, comprised mostly of galactose, arabinose, rhamnose, and glucuronic acid. This polymer is used in many fields due to non-toxicity, water solubility, and biocompatibility. In order to increase solubility of natamycin, coupling of periodate oxidized polysaccharide gum Arabic and antibiotic was performed. Resulting conjugate was characterized by UV-Vis and FT-IR data. Obtained conjugate was soluble in water.

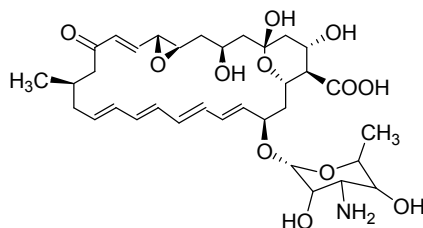


Figure 1. Structure of natamycin.

Experimental

Oxidation of gum Arabic to polyaldehyde derivative was done with sodium periodate in aqueous solution at 20 °C. Excess periodate was removed from reaction mixture by dialysis and oxidized polymer was lyophilized. Aldehyde groups in polysaccharide were determined by titration with standardized iodine solution [1]. In these conditions, sample of 50% oxidized gum Arabic was obtained. Coupling reaction between oxidized gum Arabic and natamycin was done in borate buffer (pH 9,1) in the dark, with continuous stirring, at 40 °C, during 48 h. Resulting conjugate was purified by dialysis and lyophilized.

Results and discussion

Synthesis of gum Arabic-natamycin conjugates was achieved by coupling reaction between aldehyde groups of oxidized polysaccharide and amine groups of antibiotic. Coupling reaction was monitored by UV-Vis (GBC Cintra 40 spectrophotometer) and IR (Nicolet 6700, in ATR mode) spectroscopy, by comparing spectra of oxidized polysaccharide and synthesized conjugate. UV spectra of native and oxidized gum Arabic do not have absorption in UV-Vis range (Fig.2a). After coupling reaction, spectrum of synthesized conjugate was significantly different (Fig.2b), with absorptions (λ_{\max} 294, 309, and 324 nm) slightly shifted in relation to natamycin [2]. Based on this, it can be concluded that aldehyde groups introduced in gum Arabic molecule are successfully coupled with antibiotic.

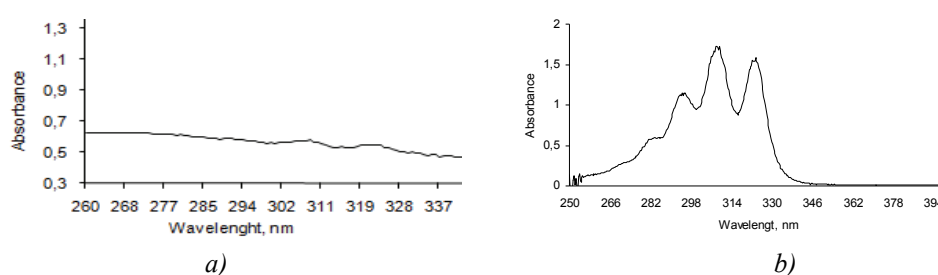


Figure 2. UV spectra of oxidized gum Arabic (a) and gum-arabic-natamycin conjugate (b).

FT-IR data suggest the chemical bonding between oxidized gum Arabic and natamycin, too. FT-IR spectrum of oxidized glycan (Fig. 3a) showed a strong band in the 3000–3500 cm^{-1} region from OH stretching, band at 2800–3000 cm^{-1} correlated to CH_2 stretching, stronger band at 1642 cm^{-1} and the weak band at about 1400 cm^{-1} corresponded to COO-asymmetric and COO-symmetric stretching, respectively. The characteristic bands of dialdehyde glycan at 1730 cm^{-1} and 880 cm^{-1} correlated to the aldehyde symmetric ($\text{C}=\text{O}$), and the hemiacetal, respectively [3]. FT-IR spectrum of the pure natamycin showed bands at 3277 cm^{-1} ($-\text{NH}_2$ deformation), 1715 cm^{-1} ($-\text{C}=\text{O}$ vibration), 1695 cm^{-1} (ester function), 1577 cm^{-1} ($\text{CH}=\text{CH}$ stretch), 1266 cm^{-1} ($\text{C}-\text{O}-\text{C}$ epoxy), 1142 cm^{-1} ($=\text{C}-\text{O}-\text{C}=\text{O}$ vibration). FT-IR spectrum of conjugate (Fig.3b) showed absorption bands characteristic for both, gum Arabic and antibiotic.

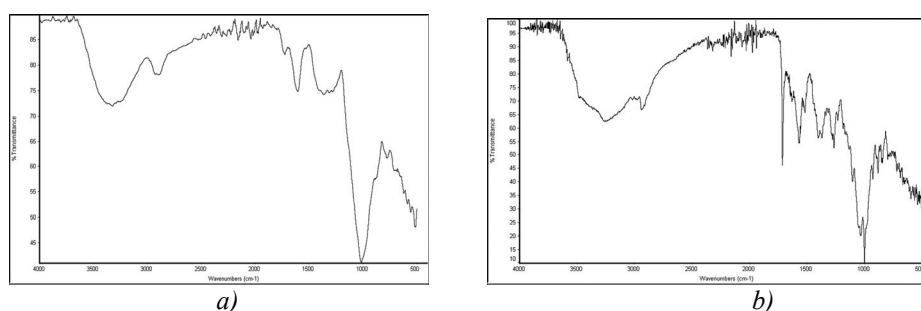


Figure 3. FT-IR spectra of oxidized gum Arabic (a) and gum Arabic-natamycin conjugates (b).

Conclusion

The synthesis of gum Arabic-natamycin conjugate was achieved by covalent coupling between oxidized polysaccharide and antibiotic. Conjugate was characterized by UV-Vis and FT-IR data. Significantly increasing the solubility in water of obtained product can be indication for potential new uses in various pharmacological applications.

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