

Modulation of the stress molecule, β -D-glucopyranosyl cholesterol, by 3-O-methylation of the sugar

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A new glycoside of cholesterol, 3-O-methyl β -D-glucopyranosyl cholesterol, was synthesized by Koenigs-Knorr glycosylation. α -D-Glucose was converted to 1,2:5,6-di-O-isopropylidene α -D-glucopyranose by reacting it with acetone in the presence of sulfuric acid and anhydrous copper sulfate. The reaction product as well as the acetylated form, 1,2:5,6-di-O-isopropylidene 3-O-acetyl α -D-glucopyranose was characterized per se spectroscopically, chemically and chromatographically. Further, the 1,2:5,6-di-O-isopropylidene 3-O-methyl α -D-glucopyranose was synthesized by methylation of di-O-isopropylidene derivative with an excess of methyl iodide/silver oxide in dimethyl formamide. Isopropylidene protecting groups were removed by acidic hydrolysis with acetic acid and 3-O-methyl D-glucose was either peracetylated with acetic anhydride-pyridine or perbenzoylated with benzoyl chloride. Peracetylated 3-O-methyl α -D-glucopyranose served as glycosylation donor, either directly or via 1-bromo 1-deoxy 3-O-methyl-tri-O-acetyl α -D-glucopyranose. Glycosylation acceptor was cholesterol, and chemical promoters were either dibutyl etherated boron trifluoride or cadmium carbonate. The glycoside of cholesterol was characterized by NMR spectroscopy. The NMR signals indicated 3-O-methyl-tri-O-acetyl β -D-glucopyranosyl cholesterol: 100.0/4.39 (d, 7.7 Hz, 1H) (C1/H1); 72.1/4.84 (dd, 8Hz, 1Hz, 1H) (C2/H2); 80.0/4.92 (t, 10 Hz, 1H) (C3/H3); 69.1/4.10 (dd, 5Hz, 7Hz, 1H) (C4/H4); 81.3/3.98 (dd, 2Hz, 10Hz, 1H) (C5/H5); 62.6/3.44 (C6/H6a); 62.6/3.39 (C6/H6b); 58.3/3.29 (s, 3H) (CH₃ etheric group); 72.0/3.46 (C3/H3 cholesterol); 122.1/5.26 (d, 5Hz) (C6/H6 cholesterol); 11.99/0.58 (C18/H18 cholesterol); 18.86/0.90 (C19/H19 cholesterol). Acyl protecting groups were removed by Zémpfen hydrolysis. The glycosylation product gave 3-O-methyl-D-glucose and cholesterol by acidic hydrolysis.

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Pharmaceutical equivalence of some injectable gentamicin generics used in veterinary practice in Nigeria

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Gentamicin is an aminoglycoside antibiotic used in the treatment of infections caused by gram-negative aerobic bacterial organisms in humans and animals. In Nigeria, there is an array of multisource generic versions of injectable gentamicin sulphate in the drug markets. There is a high prevalence of counterfeit and substandard drugs in the third world countries with consequent effect on their therapeutic efficacy and safety. The aim of this study was to investigate pharmaceutical equivalence of some of these generics used in veterinary practice in Nigeria. About 20 generics of injectable gentamicin sulphate were sampled randomly across Nigeria but 15 were analyzed for identity and potency. Identity test was done using Fourier transform infra-red spectroscopy and the spectral for each product compared with that of the USP reference standard for similarity. Microbiological assay using agar diffusion method with *E. coli* as a test organism on nutrient agar was employed and the respective diameters of bacterial inhibition zones obtained after 24 hour incubation at 37°C. The percent potency for each product was thereafter calculated and compared with the official specification. None of the generics is produced in any African country. About 75% of the products are imported from China whereas 60% of the veterinary generics are manufactured in Holland. Absorption spectra for the reference and test samples were similar. Percent potencies of all test products were within the official specification of 95-115%. Nigeria relies solely on imported injectable gentamicin sulphate products. All sampled generic versions passed both identity and potency tests. Clinicians should ensure that drugs are used rationally since the converse could be contributing to the therapeutic failures reported for most of these generics. Bioequivalence study is recommended to ascertain their interchangeability when parenteral extra venous routes are indicated.

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