MUTAGENIC ACTIVITY OF QAS DERIVATIVES OF GLYCOPYRANOSIDES

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Quaternary aminium salts (QAS) are extensively used in various applications. They are present in fabric softeners and corrosion inhibitors, they act as fungicides, pesticides and insecticides, they reveal antibacterial and antifungal activities employed in antimicrobial drugs, and they are ingredients of shampoos and hair conditioners. Therefore, global use of QAS in industry, agriculture, healthcare and domestic approaches is doubtless. Although toxicity of some QAS has been reported, majority of these compounds were reported as non-toxic or of low toxicity. Therefore, QAS are generally believed to be safe [1,2].

A series of quaternary aminium salts (QAS) have been synthesized in reaction of n-bromoalkyl 2',3',4',6'-tetra-*O*-acetyl-β-D-glycopyranoside and n-bromoalkyl 2',3',4',6'-tetra-*O*-acetyl-α-D-glycopyranoside with tertiary amines: pyridine and trimethylamine (Figure 1).

In order to examine genotoxic potential of newly synthesized *N*-[n-(D-glycopyranosyloxy) alkyl]aminium salts, we used two different bacterial mutagenicity assays. First of them, known as an Ames test, employs histidine dependent *Salmonella typhimurium* strains and is recognized as the most commonly used short-term bacterial mutagenicity assay, not only for scientific purposes, but also applied in analysis of newly introduced chemicals by regulatory agencies (Figure 2). In the second assay marine *Vibrio harveyi* A16 dim mutant is used. Upon the addiction of a genotoxic compound a particular fraction of bacteria regain bioluminescence ability, which serves as a measure of a mutagenic effect (Figure 3).

One of analyzed compounds, *N*-[11-(2',3',4',6'-tetra-*O*-acetyl-α-D-glucopyranosyloxy) undecyl]-*N,N,N*-trimethylaminium bromide (**αT11GAc**) exhibited pronounced mutagenic activity in the Ames test in lower concentrations, for concentrations 0.5 mg and 2 mg it exhibited bacteriostatic activity. The pictures of bacterial growth are presented in Figure 4.

For two other compounds, *N*-[11-(β-D-glucopyranosyloxy)undecyl]pyridinium bromide (**βP11G**) and *N*-[2-(2',3',4',6'-tetra-*O*-acetyl-β-D-galactopyranosyloxy)ethyl]pyridinium bromide (**βP2G'Ac**), a weak mutagenic effect in the Ames test was observed. Remaining compounds were assessed as non-mutagenic. On the other hand, *V. harveyi* bioluminescence assay demonstrated a pronounced mutagenic effect in a broad range of compounds concentrations, which suggest higher sensitivity of *V. harveyi* (two examples of results presented on Figure 2) test in comparison to the Ames test. These findings demonstrate that *N*-[n-(D-glycopyranosyloxy)alkyl]aminium salts can be genotoxic and reveal the need for their further profound testing, especially with test systems which can provide high sensitivity, such as *V. harveyi* bioluminescence assay.

A part of results concerning *N*-[2-(D-glycopyranosyloxy)ethyl]aminium brimides was published in two papers [3, 4].

Figure 1. Structures of QAC derivatives of sugars

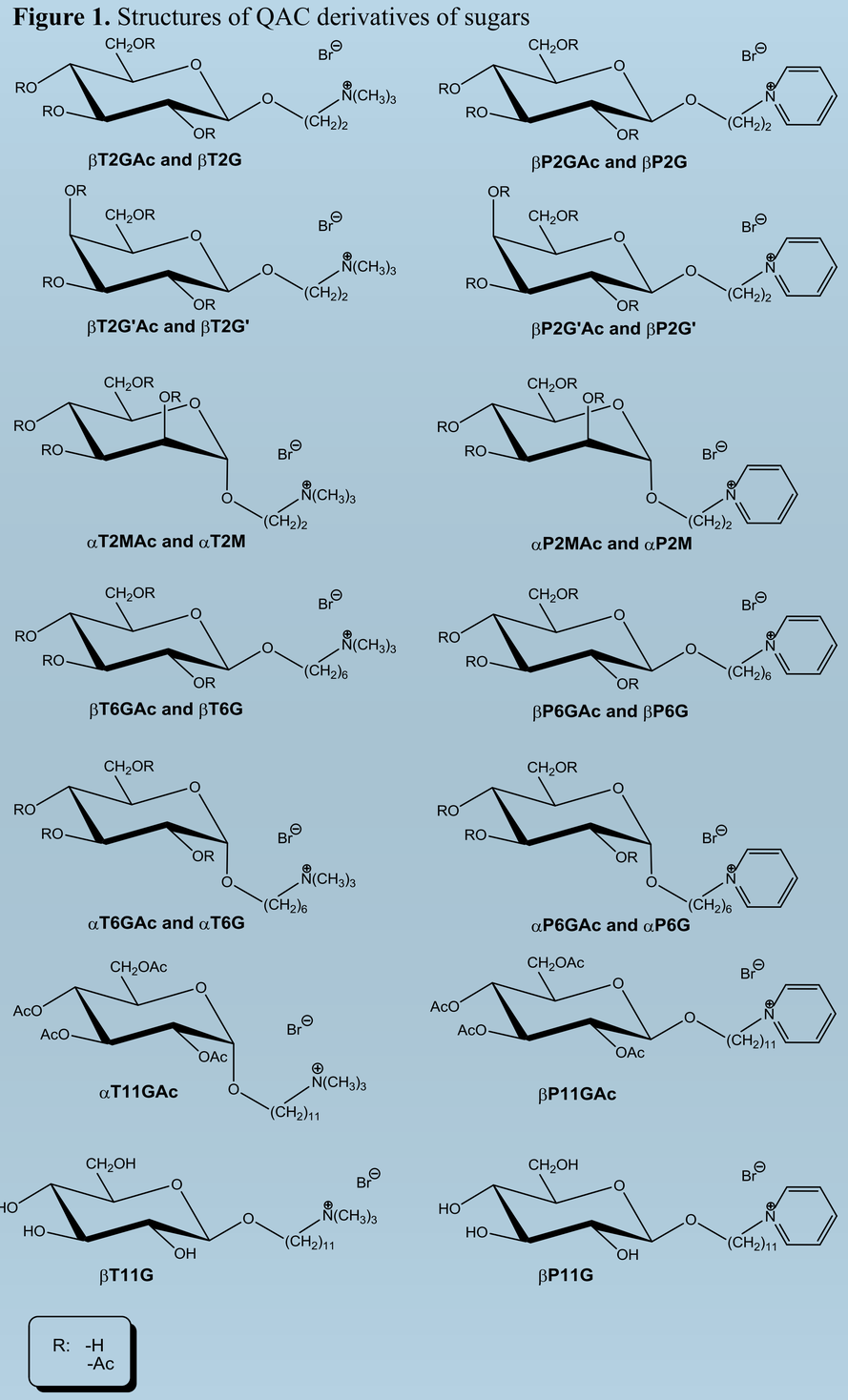


Figure 3. *Vibrio harveyi* A16 results for: **αT2M** and **αP2M** (C – negative control, ICR191 - model mutagen, 0.1mg/plate)

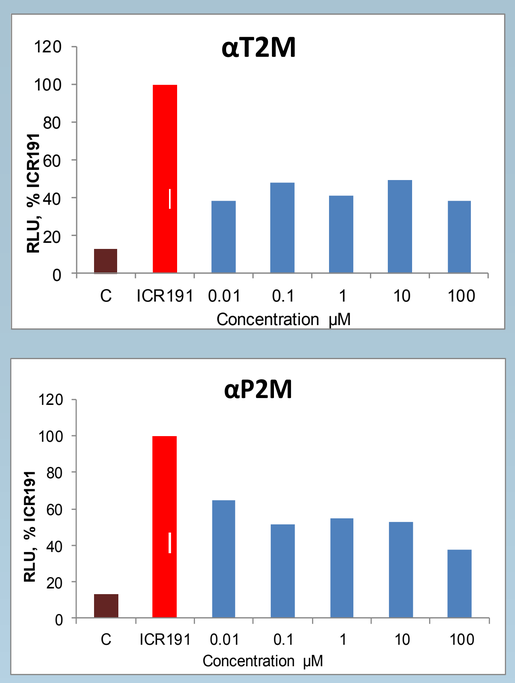


Figure 2. Ames test results for quaternary aminium bromides in concentration 0.1mg/plate (C – negative control, ICR191 - model mutagen, 0.1mg/plate)

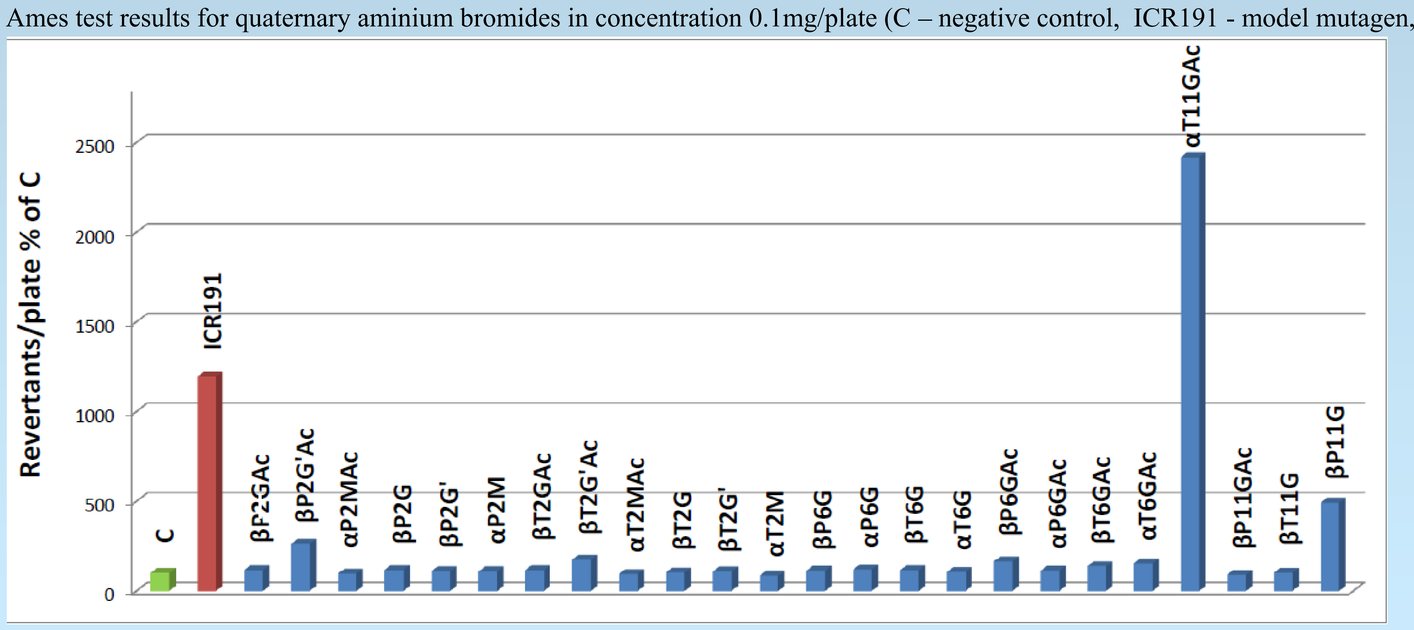
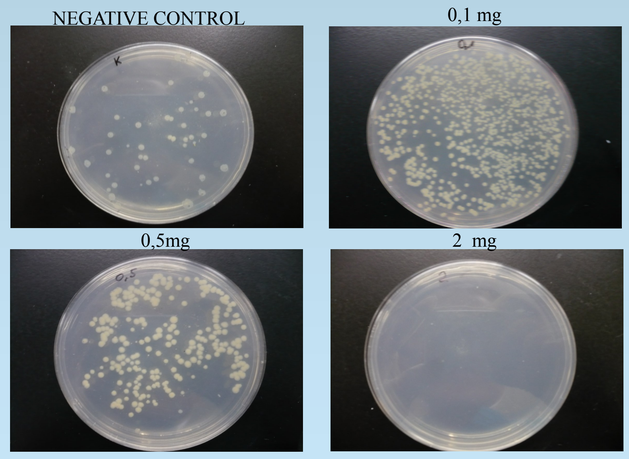


Figure 4. Revertants for **αT11GAc**



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Acknowledgement:
This work was partially financed by grant: BMN 538-8451-B006-13 and DS/530-8451-D193-12
The publication is financed from European Social Fund in as a part of the project " Educators for the elite - integrated training program for PhD students, post-docs and professors as academic teachers at University of Gdansk" within the framework of Human Capital Operational Programme, Action 4.1.1, Improving the quality of educational offer of tertiary education institutions.