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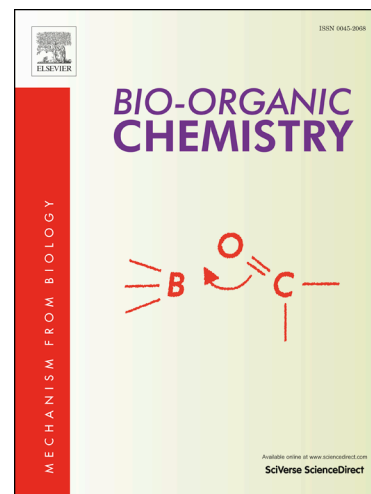
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**Design, synthesis and biological evaluation of novel ureido benzenesulfonamides incorporating 1,3,5-triazine moieties as potent carbonic anhydrase IX inhibitors**

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**Abstract**

A series of novel ureido benzenesulfonamides incorporating 1,3,5-triazine moieties were obtained by reacting 4-isocyanato-benzenesulfonamide (**2**) with 2-amino-4,6-dichloro-1,3,5-triazine (**4**). The 4-(3-(4,6-dichloro-1,3,5-triazin-2-yl)ureido) benzenesulfonamide (**5**) was subsequently derivatized by reaction with various nucleophiles such as, morpholine, ammonia, methyl amine, dimethyl amine, and piperidine. The ureido benzenesulfonamides incorporating triazinyl moieties were investigated as inhibitors of four selected physiologically relevant human carbonic anhydrase (hCA, EC 4.2.1.1) isoforms, namely, hCA I, II, IX, and XII which are involved in various diseases such as glaucoma, epilepsy, obesity and cancer. The membrane-bound tumor-associated isoform hCA IX was potently inhibited with these compounds with  $K_i$ s in the range of 0.91 to 126.2 nM. Specifically, compound **7j** showed great potency against hCA IX with sub-nanomolar  $K_i$  of 0.91 nM. Since hCA IX is a validated drug target for anticancer agents, these isoform-selective and potent inhibitors may be considered of interest for further medicinal/pharmacologic studies.

**Key words:** Ureido benzenesulfonamides, 1,3,5-triazine moiety, Carbonic anhydrase, Isoforms, Isoform-selective inhibitor, cancer

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