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Intraocular pressure lowering effect and structure-activity relationship of imidazo[1,2-a]benzimidazole and pyrimido[1,2-a]benzimidazole compounds in ocular normotensive rats: Insight on possible link with hypotensive activity

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Intraocular pressure lowering effect and structure-activity relationship of imidazo[1,2-a]benzimidazole and pyrimido[1,2-a]benzimidazole compounds in ocular normotensive rats: insight on possible link with hypotensive activity

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Abstract: In an effort to find new ocular hypotensive drug candidates, a total of 27 condensed benzimidazoles based compounds were screened. This study was done in normotensive rats and rebound tonometry was used to estimate IOP. All compounds were topically applied as a single drop, unilaterally, at 3 different concentrations (0.1%, 0.2% and 0.4%). The contralateral eye was instilled with vehicle and served as control. The IOP reduction was measured up to 6 hours. We observed that, with a single topical instillation, four compounds RU 551, RU 555, RU 839 (pyrimido[1,2-a]benzimidazole), and RU 615 (imidazo[1,2-a]benzimidazole) showed significant IOP lowering activities in ocular normotensive rats. All other compounds showed none, weak and inconsistent IOP lowering effect. The relationship between ability of IOP lowering and hypotensive activities was shown. According to the pharmacophore analysis, the class of pyrimido[1,2-a]benzimidazole is more promising than the class of imidazo[1,2-a]benzimidazole as a source of compounds with high IOP lowering activity. Pharmacophore analysis also showed that the critical features of high IOP lowering activity are methoxyphenyl and [phenyl]alkyl fragments, and non-conjugated six-membered heterocyclic ring.

Keywords: Drug screening, glaucoma, intraocular pressure, imidazo[1,2-a]benzimidazoles, pyrimido[1,2-a]benzimidazoles, structure-activity relationship

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