Clin Pharmacol Biopharm 2016, 5:4(Suppl)
http://dx.doi.org/10.4172/2167-065X.C1.023

Design, synthesis and biological evaluation of novel 2-phenyl-1-benzopyran-4-one derivatives as potential poly-functional anti-Alzheimer's agents

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Development of Multi-Target Directed Ligands (MTDLs) has emerged as a promising approach for targeting complex etiology of Alzheimer's disease (AD). Following this approach, a new series of 2-phenyl-1-benzopyran-4-one derivatives were designed, synthesized and biologically evaluated as inhibitors of acetylcholinesterases (AChEs), advanced glycation end products formation (AGEs) and also for their radical scavenging activity. The *in vitro* studies showed that the majority of synthesized derivatives inhibited acetylcholinesterase (AChE) with IC_{50} values in the low-micromolar range. Among them, inhibitors 7h, 7k and 7a, strongly inhibited AChE, with IC_{50} value of 6.33, 7.56 and 11.0 nM, respectively, and were more potent than the reference compound donepezil. Moreover, the molecular docking study displayed that most potent compounds simultaneously bind to catalytic active site and peripheral anionic site of AChE. Besides, these compounds also exhibited greater ability to inhibit advanced glycation end products formation with additional radical scavenging property. Thus, 2-phenyl-1-benzopyran-4-one derivatives might be the promising lead compound as potential poly-functional anti-Alzheimer's agents.

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Assessment of adhesion response to 3D printed materials for ophthalmic device development

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Introduction & Aim: Glaucoma is the leading cause of irreversible visual impairment worldwide. Glaucoma surgical devices fail due to a scarring response that resulted in fibrous encapsulation surrounding the device preventing aqueous humor drainage. 3D printing technology has the potential to develop personalized ophthalmic devices or organs with improved cost effectiveness and productivity. Limited experimental data exists as to the biocompatibility response of 3D printed photopolymers. We performed cell adhesion and protein adsorption studies of 3D printed photopolymers compared to materials used in current ophthalmic devices (silicone, polytetrafluoroethylene (PTFE) and poly (methyl methacrylate) (PMMA)) to assess 3D printed materials as a potential route for ophthalmic device development.

Methods: 3D printed materials (n=6) were developed using a high-resolution, desktop stereo-lithography (SLA) 3D printer and compared to materials used in current ophthalmic devices. Protein adsorption was quantified using a micro bicinchoninic acid (micro BCA) assay and fluorescein-conjugated bovine serum albumin (FITC-BSA) adsorption. Cell adhesion (monocytes, fibroblasts) was assessed using alamarBlue, CyQUANT and Live/Dead assays. Data were compared using a two-tailed unpaired t-test.

Results: 3D printed materials demonstrated low cell adhesion and protein adsorption. Results were similar to those found with materials used in current ophthalmic devices ($P>0.05$). However, it was noted that 3D printed materials demonstrated increased cytotoxicity ($P<0.05$).

Conclusion: 3D printed photopolymer materials demonstrated a similar biocompatibility response to currently used materials and may allow for the development of customizable ophthalmic devices or organs. Subsequent testing will determine the adhesion response to 3D printed materials containing anti-scarring agents.

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