Research Paper

Synthesis of Some Novel 5-Substituted Arylidene – 2, 4-Thiazolidinediones as Bioactive Agents

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ABSTRACT: A series of 5-substituted arylidene-2,4-thiazolidinedione derivatives were synthesized from 2,4-thiazolidinedione and substituted aromatic aldehydes. The synthesized title compounds were screened for their in-vivo anti-inflammatory and analgesic and in-vitro antioxidant activities as per standard protocols. All the compounds were found to possess significant activities.

KEYWORDS: 2,4-thiazolidinediones; Anti-inflammatory activity; Analgesic activity; Antioxidant activity

Introduction

Thiazolidinedione (TZD) pharmacophore has been the subject of immense research because of its deep involvement in regulation of various physiological processes (Komers and Vrana, 1998). Thiazolidinediones with substitution at 5th position show remarkable antidiabetic activity binding with PPARγ (Mourao et al., 2005). Not only this, they show other activities like aldose reductase inhibition (Dundar and Bauer, 2008), anti-inflammatory (Dandona et al. 2003), analgesic, antioxidant (Matsumoto et al., 1997, Bhattacharya and Hossain, 2007), and antimicrobial activity (Mulwad and Mir, 2009). TZDs act by binding to PPARγ (Peroxisome Proliferator Activated Receptors γ), a group of receptor molecule inside the cell nucleus (Lehmann et al., 1995). Binding of TZDs with PPARγ has been suggested to play down regulatory role in treatment of inflammatory disorders (Delerive et al., 2001; Daynes and Jones, 2002). TZDs give potential anti inflammatory activity by inhibiting monocyte/macrophage activation and expression of inflammatory molecules such as interleukin IL-1β, IL-6, and tumour necrosis factor (TNF-α) (Jing and Ting, 1998; Ricote and Li, 1998). In-vitro and in-vivo anti inflammatory activities of TZDs, troglitazone and rosiglitazone have been reported (Dandona at al., 2003). Thiazolidinediones are a class of insulin-sensitizing agents. They inhibit intracellular free radical overproduction. In particular, they inhibit the same pathways involved in hyperglycaemia-derived oxidative stress, particularly iNOS and NF-κB. Studies in animal models suggest that thiazolidinediones can reduce oxidative stress, independent of their ability to reduce hyperglycaemia (Da Ros et al. 2004).

Keeping all these facts in view, an attempt has been made to prepare some compounds of the 5-substituted-arylidene-2,4-thiazolidinediones substituted either on the benzylidene or benzyl moiety. Synthesis of the compounds was confirmed by physical and spectral characterization. Compounds thus formed were subjected to further evaluation for their in-vivo anti-inflammatory and analgesic activity and in-vitro antioxidant activity by using standards protocols.

Materials and Methods

5-substituted arylidene-2, 4-thiazolidinediones were prepared by Knoevenagel condensation of commercially available 2, 4-thiazolidinedione with meta- and para-substituted benzaldehydes by using piperidine as base.

A mixture of 2, 4-thiazolidinedione (0.01 mol), substituted aldehydes (0.01 mol), piperidine 1.4 g and ethanol 150 ml was refluxed for 16-24 hrs. The reaction mixture was poured into water and acidified with acetic acid to give final product 1(a)-1(c) as solids which were recrystallized from methanol (Bruno et al., 2002). The progress of the reaction was monitored by TLC. The synthesized compounds were characterized by spectral data (Pavia et al., 2007, Kalsi, 2004) as shown in Table 1.

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