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SYNTHESIS AND INVESTIGATION OF ANTIDIABETIC RESPONSE OF NEW COUMARIN DERIVATIVES AGAINST STREPTOZOTOCIN INDUCED DIABETES IN EXPERIMENTAL RATS

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A new series of coumarin analogs (1a – 1g) were designed and synthesized. The chemical structures of all compounds were elucidated by IR, ^{1}H NMR, ^{13}C NMR, and mass spectroscopy techniques. The synthesized compounds were investigated for their anti-diabetic activity against streptozotocin (STZ) induced diabetes in rats. The albino rats were selected to observe the oral glucose tolerance test (OGTT) by oral intake of aqueous glucose solution (4 g/kg body weight) in normal rats and estimate the blood glucose level after administration of compounds 1a – 1f at 50 and 100 mg/kg, and standard drug glibenclamide at 0.6 mg/kg body weight. Antidiabetic activity was studied by estimating the blood glucose level in diabetic rats. The results showed that all the synthesized coumarin analogs 1a – 1g exhibited antidiabetic potential. Compounds 1a – 1f produced eminent antidiabetic effects in STZ induced diabetic rats.

Keywords: coumarin; antidiabetic; streptozotocin; glucose; glibenclamide.

1. INTRODUCTION

Coumarin belongs to benzopyrone family as a principal member and consists of a benzene nucleus fused with α-pyrone ring structure (benzo-α-pyrone). Generally, 4-hydroxy coumarin and 7-hydroxy coumarin are basic scaffolds for the substitution and derivatization to design new drug candidates [1]. Coumarin ring systems are already established moiety that possess numerous biological and pharmacological potentials such as anticoagulant [2], anti-HIV [3], antimicrobial [4, 5], anti-inflammatory [6], anticancer [7, 8], anti-tuberculous [9], anti-convulsant [10], anti-parkinsonian [11], anti-alzheimer [12], and anti-diabetic [13].

Diabetes mellitus type II (DM-II) is a worldwide health problem of middle and older age people, but presently the rate of DM-II in young generation is augmenting. DM-II is common due to dietary modification, lifestyle modification, and genetic components. The most common signs of DM-II are polyphagia, weight loss, polyuria and polydipsia. It conjointly includes fatigue, blurred vision and peripheral neuropathy. Despite various synthetic approaches, herbal medicines are also used in the management of DM-II [14 – 17]. Various active chemical constituents such as aegeline alkaloids from *Aegle marmelos* [18], scoparone from *Artemesia capillaris* [19], and glycyrin from *Glycyrrhiza uralensis* have been isolated from plants that are widely employed for the treatment of DM-II and other metabolic disorders [20]. After considering the basic lead structure of the aforementioned phytochemicals and basic structure requirements for anticipated pharmacological activity, it was predicted that the synthesized 7-hydroxy coumarin derivatives 1a – 1g (Fig. 1) should possess anti-diabetic properties.

2. EXPERIMENTAL

2.1. Materials and Methods

All the starting materials, reagents and solvents were purchased from central drug house (CDH, New Delhi, India). Melting points were determined by open capillary method

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