

Newer approaches to the discovery of glitazones

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Thiazolidines (TZDs) or glitazones are one of the important classes of insulin sensitizers used in the management of type 2 diabetes mellitus. These agents, however, suffer from some serious side effects such as fluid retention, weight gain, congestive heart failure, bone fracture and possibly bladder cancer, which resulted in their withdrawal from clinical use. The TZDs that were withdrawn from the clinical use were developed at the time when enough scientific data were not available on the structure and the transcriptional mechanisms of peroxisome proliferator activated receptors (PPARs). Recent advances in the understanding of structure and function of PPARs, however, has led to more rationalized approaches to develop these agents. This presentation discusses the various approaches that have been made to develop newer glitazones devoid of the problems associated with current TZDs. These approaches are based on the structural considerations of both the ligands and the receptors and also on the profile alterations of the ligands.

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