

# Development of Mammalian Cell-Based Assay System to Screen For PPAR $\gamma$ Ligands From Natural Products



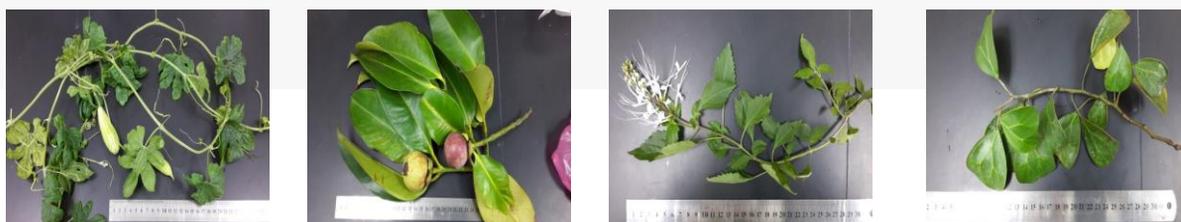
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Insulin resistance is the symptom of reduced insulin sensitivity in the body tissues towards circulating glucose, resulting in prolonged high blood sugar level. Consequently, this results in type II diabetes mellitus in the long run, which brings further complications on the sufferers affecting the micro vessels (i.e retinopathy, nephropathy and neuropathy) and macro vessels (i.e heart disease such as coronary artery disease).

Thiazolidinedione (TZD) drugs which are effective and currently used for the treatment of insulin resistance were recognized as potent peroxisome proliferator-activated receptor  $\gamma$  (PPAR $\gamma$ ) ligands. However, adverse side-effects accompanying this class of drugs such as induction of hepatotoxicity, cardiovascular events including heart failure, fluid retention and haemodilution outweigh its benefit. Hence, identification of new, natural PPAR $\gamma$  ligands from the natural products as alternatives for the treatment of insulin resistance is essential.

In this study, a mammalian cell-based assay system was developed to screen for potential PPAR $\gamma$  ligands from natural products. This reporter gene based assay utilizes transient transfection of two reporter plasmids; pAcox PPREx3-Tk-Luc and pRL-CMV (as internal control), and two expression plasmids; pSV Sport PPAR $\gamma$  and pSV Sport RXR $\alpha$  in HepG2 cells. The assay successfully distinguished the presence of PPAR $\gamma$  ligands when tested with TZD drug as well as some plant extracts containing natural PPAR $\gamma$  ligands including *Momordica charantia* which is known to have ethno-pharmacology history in type II diabetes treatment. Other plant extracts were also identified to contain potential natural ligands of PPAR $\gamma$  including *Garcinia mangostana*, *Orthosiphon aristatus* and *Ficus deltoidea*. Some natural compounds screened using this assay system, were also verified for their glucose uptake ability. To conclude, we have developed a mammalian cell-based assay system to screen for natural PPAR $\gamma$  ligands in an effort to identify new candidate compounds or extracts for use in the treatment of type II diabetes mellitus.



**Figure 1** : Showing some parts taken from *Momordica charantia*, *Garcinia mangostana*, *Orthosiphon aristatus* and *Ficus deltoidea* plants.