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In silico identification of *Jatopha gossypifolia* L. flavonoids as aldose reductase inhibitors in diabetes mellitus

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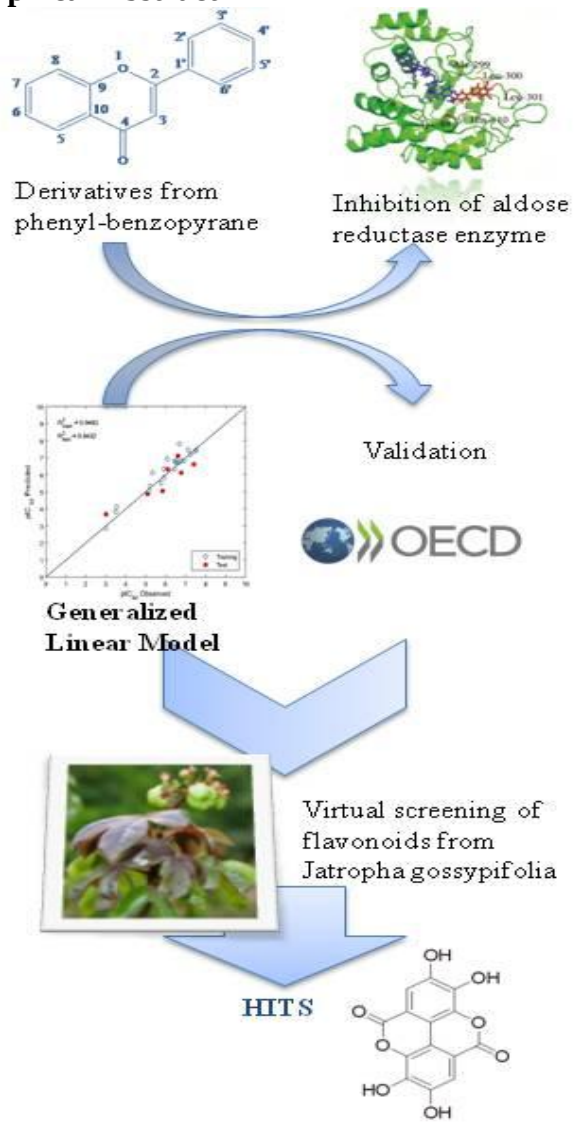
Graphical Abstract



Abstract.

Diabetes mellitus is a common chronic metabolic disease that constitutes a risk factor to patient infected by Covid-19. Aldose reductase enzyme catalyzes the metabolic glucose-sorbitol conversion for the polyol pathway in diabetic conditions. The accumulated sorbitol in the tissues has been reported to be responsible for diabetic complications such as cataracts, retinopathy, neuropathy, and nephropathy. Inhibitors of aldose reductase are considered as therapeutic target in prophylaxis and treatment of these affections. A particular case, have been studies the flavonoids isolated from fruits, vegetables and medicinal plants. In the current paper we development a Generalized Linear QSAR model using MATLAB and molecular descriptor implemented in DRAGON software. A result shows a model adjusted whit R^2 of 0.948. The model was extensively validated according to OECD regulatory principles by mean of internal and external validation exercises. In addition, the applicability domain was obtained to warranty the trustworthy of the predictions. Due to it predictive power (R^2ext = 0,943) the model was used to predict the ALR2

	inhibition by the flavonoids reported in *Jatopha gossypifolia* L. The ellagic acid was the most promising metabolite (pIC_{50} predicted = 12.69), which is into the applicability domain and have drug-like properties for oral administration. Finally, we can conclude that proposed tools are useful to the quick and economic identification of drug potential candidates against ALR2 in diabetic complications.

Conclusions

The QSAR-GLR model obtained, simple and robust, correlates satisfactorily the chemical structure of natural flavonoids with the inhibitory activity of the enzyme aldose reductase. The validity of the model according to the OECD standards supports its applicability to predict the activity of new flavonoids of natural or synthetic origin. The *Jatropha gossypifolia* L. species has flavonoids with high potential as inhibitors of the enzyme aldose reductase, which suggests its possible use in late complications of diabetes mellitus and supports its ethnomedicinal use in this pathology. The biflavonoid ellagic acid was shown to be the most promising inhibitor of the enzyme aldose reductase, so the use of medicines, nutritional supplements and foods that contain it can contribute to the management of complications of diabetes mellitus.

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