**DPP-4 inhibition mediated antidiabetic potential of phytoconstituents of an aqueous fruit extract of *Withania coagulans* (Stocks) Dunal: *in-silico*, *in-vitro* and *in-vivo* assessments**

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**Abstract**

The DPP-4 inhibition is an interesting target for the development of antidiabetic agents which promotes the longevity of GPL-1(Glucagon-like peptide 1). The current study was intended to assess DPP-4(Dipeptidyl Peptidase-4) inhibition mediated antidiabetic effect of phytocompounds of an aqueous fruit extract of *Withania coagulans* (Stocks) Dunal by *in-vitro*, *in-silico* and *in-vivo* approaches. The phytoconstituents screening was executed by LCMS (Liquid Chromatography with tandem mass spectrometry). The *in-vitro* and *in-vivo*, DPP-4 assays were performed by using available kits. The *in-vitro* DPP-4 activity was inhibited up to 68.3% by the test extract. Accordingly, *in-silico* determinations of molecular docking, molecular dynamics and pharmacokinetics were performed between the target enzyme DPP-4 and leading phytocompounds. The molecular dynamics authenticated the molecular docking data by crucial parameters of cytosolic milieu by the potential energy, RSMD (Root Mean Square Deviation), RSMF (Root Mean Square Fluctuation), system density, NVT (Number of particles at fixed volume, ensemble) and NPT (Number of particles at fixed pressure, ensemble). Accordingly, ADMET predictions assessed the druggability profile. Subsequently, the course of the test extract and the sitagliptin (positive control), instigated significant (*p* ≤ 0.001) ameliorations in HOMA indices and the equal of antioxidants in nicotinamide-streptozotocin induced type 2 diabetic animal model. Compassionately, the histopathology represented increased pancreatic cellular mass which caused in restoration of histoarchitectures. It has been concluded that phytoconstituents in *W. coagulans* aqueous fruit extract can regulate DPP-4, resulting in improved glucose homeostasis and enhanced endocrinal pancreatic cellular mass.

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**KEYWORDS:**

* [*Withania coagulans* (Stocks) Dunal](https://www.tandfonline.com/keyword/Withania+coagulans+%28Stocks%29+Dunal)
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**Disclosure statement**

No potential conflict of interest was reported by the authors.

**Ethical approval**

The Institutional Animal Ethical Committee (IAEC), Department of Zoology, JNVU, Jodhpur approved the protocols of current study as per CPCSEA norms (Reg. No.1646/GO/a/12/CPCSEA valid up to 27.03.23).

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HR & BPS- Concept and Supervision, PKB & CA– *In-silico* investigation, PK- Phytochemistry, AK &AP Molecular Dynamisc, GS-Drafting & botanical Authentication,

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