PREPARATION, PHYTOCHEMICAL INVESTIGATION AND EVALUATION OF ANTI-DIABETIC ACTIVITY OF POLYHERBAL EXTRACT

Thesis submitted in partial fulfilment for the Award of Degree

Doctor of Philosophy

By

Amit Kumar Singh

DEPARTMENT OF PHARMACEUTICAL ENGINEERING & TECHNOLOGY
INDIAN INSTITUTE OF TECHNOLOGY
(BANARAS HINDU UNIVERSITY)
VARANASI – 221005
INDIA

Roll No- 18161516 **Year 2024**

CHAPTER 7

Conclusion

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Several bioactive compounds were identified in the ethanol extract of PHE screened through GC–MS analysis that could be useful in treating various diseases. As a result of this study, it can be concluded that plant-based therapies can play an important role in protecting against free radical damage. Each ingredient medicinal plant of PHE showed synergistic antioxidant potential. PHE wasfound to be highly effective and proved its anti-inflammatory activity through an*in vitro*study.

The potential activity of PHE against diabetes was found to involve the bioactive compounds and common genes in the network pharmacology study. The most important finding, however, was that PHE is effective in warding off diabetes and that ATA of PHE is a key active component and TNF is a key hub gene. The *in-vitro* antidiabetic activity of PHE confirmed the bioinformatic study, which highlighted the key signaling pathways enriched with hub genes thatstimulate signaling pathways like MAPK and PI3K/AKT, which may enhance insulin receptor (IR) autophosphorylation.The phenols and flavonoids were identified and found to be enriched in PHE, which may be effective even at lower doses. The acute and sub-acute testing of PHE in this study suggests that it could be used safely, allowing patients to take their medications less frequently and for a shorter period of time.

In summary, PHE reduces resistance to insulin in STZ-induced diabetic rats because it is rich in kaempferol, quercetin, and rutin, which were measured in the HPTLC investigation. Because of the enrichment of these phenolic and flavonoid substances, the putative molecular mechanisms of PHE are a rise in glucose absorption, raised insulin levels, and a decline in pancreatic β-cell death in diabetic rats. In this study's network pharmacology-based investigation of the key metabolites produced by the gut microbiota in mitigating DM, the antidiabetic effect of PHEwas established. Ursodeoxycholic acid, a key metabolite of the gut microbiome in bioinformatic studies for antidiabetic activity, was found to be able to act as

an antagonist of the AGE-RAGE signaling pathway in diabetic complications or other up-regulated TNF signaling pathways.In this study, the binding affinity of ursodeoxycholic acid was found to be effective and stable for core common target genes (MMP2, MMP14, and CASP3) against DM involved in the pathways by MDT. In this study, we found that the PHE-microbiota-metabolite-signaling pathways-targets-networks may be significant essential parts and distinguishing characteristics for the management of DM.

In conclusion, the presence of several bioactive substances such as chebulic acid, ellagic acid, gallic acid, andrographolide, berberine, kaempferol, quercetin, luteolin, rutin, apigenin, and others in PHE suggested that it could alleviate the hyperglycemia in DM rats. Furthermore, PHE was able to change the gut microbiome and enhance SCFAs, both of which were significant in the pathophysiology of DM. Finally, we hypothesized that SCFA-producing as well as anti-inflammatory bacterial genera like *Lactobacillus*, *Oscillospira*, *Prevotella*, *Desulfovibrio*, [*Prevotella*], and *Bacteroides* were involved in PHE's beneficial effects on DM rats. Specifically, the enrichment of bacterial strains like *Prevotella copri* and*Lactobacillus hamster* and the decline in relative abundance of *Bifidobacterium pseudolongum*, *Ruminococcus bromii*,and*Blautia producta* through PHE treatment produce health benefits because the generated metabolites increase epithelial barrier function, improve gut permeability, inhibit inflammation, reduce insulin resistance, and reduce the severity of DM by modulating the multiple metabolic pathways with multiple targets involved. In this study,we found unanticipated impacts of PHE's systemically hypoglycemic effects using dual therapies such as PHE phytochemicals, regenerated gut microbiota, and associated SCFAs that treated DM. Finally, because PHE regulates the hyperglycemic index and other related biochemical indices in diabetic rats, as seen earlier in the bioinformatic study, it may be a great source of natural anti-diabetic drugs.In the future, using a mechanistic approach to study the gut microbiota's anti-diabetic properties in vivo and apply them to clinical practice may help treat DM.

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