Highthroughput Screening and Identification of Antidiabetic Compounds from a Polyherbal Unani Formulation "Sofoof-e- Ziabetus" and Its Constituents

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SUMMARY

Diabetes is known since the time of yore where symptoms of Diabetes were described. This disease has apparently beleaguered man for a very long time and the writings from the earliest civilizations (Asia Minor, China, Egypt and India), Mainy researchers and scholers performed the research work to find out the curable drugs without any side effect but they could not get the success till date. Various herbal plants are studied as single drugs and compound formulation and validated scientifically to carry out the safe antidiabetic drugs but till now such type of drug not found.

SZ-I, SZII and its ingredients were used since long time but scientifically not validated.

Qualitative analysis of the SZ-I, SZ-II and its ingredients were carried out in which organoleptic characters and Physico-Chemical Standards were studied. The HPTLC was also performed and Rf values were reported. The HPTLC analysis helped in the establishing a HPTLC fingerprinting profile to authenticate the formulation and ingredients and quality control analysis as a standard reference.

The total phenolic and flavonoid contents of SZ-I, SZ-II, Gilo, Gurmar, Habbul-as, Samage-Arabi and Tukhm-e-Hummaz were analyzed, phenolic and flavonoid contents were found to be higher concentration in SZ-I, SZ-II and Tukhm-e Hummaz among all test drugs and presence of higher concentration indicated the higher potential effect against Diabetes mellitus.

The extracts of plant material were tested for their antioxidant potential by DPPH scavenging activity and α-amylase, α-glucosidase enzymes inhibitory activity. Maximum DPPH scavenging activity, α-amylase and α-glucosidase inhibition potential were observes at higher concentration of 1000 μg/ml in SZ-I (alcoholic), SZ-II (alcoholic), Hummaz (aqueous) and Habbul-as

(aqueous), with compression of the standard control of ascorbic acid and acarbose respectively that means they all samples have more action potential in compression to others.

LC/MS analysis of test drug done to study the complete metabolomic profiling. A total of 43, 34, 26, 42 and 41 metabolites were separated and tentatively identified for Hummaz, Habbul-as, Gurmar, SZ-I and SZ-II respectively from the database.

HPTLC-MS bioautograph of test drugs was performed to search the metabolite compounds which are responcible for antidiabetic activity.

Antidiabetic activity of alcoholic extract of SZ-I, SZ-II and aqueous extract of Hummaz was evaluated using parameters of FBS and PPG. In initial stage there was no significant reduction in FBS and PPG with comparison of negative control, after 14^{th} day FBS and PPG gradually decreased, in test drug and standard drug group but at the end of 28 days reduction of FBS and PPG was observed prominently in SZ-II HD and Hummaz HD with comparison to negative control and it was considered as highly significant ($P<0.001$ vs negative control).

OGTT was also performed to check the hypoglycemic activity of test drug, After 3 h of glucose administration the maximum fall in blood glucose level observed with the dose of 800 and 500 mg /Kg of SZ-II HD and Hummaz HD respectively it was 56.7% and 53%, respectively ($P<0.001$ vs negative control), moreover metformin the reference drug produced a fall of only 57%. Lesser fall down of plasma glucose was observed in the remaining groups.

Antihighperlipidimic activity of test drugs was evaluated using lipid profile parameters (TC, TGL, LDL and HDL). Values of TC, TGL, LDL significantly increased in negative control with comparison of plain control, the all parameters were prominently decreased in test drug SZ-II HD and Hummaz HD (800mg/kg and 500mg/kg respectively) and it was considered highly significant ($P<0.001$ vs negative control) while in other remaining groups all parameters decreased significantly.

Individuals with type 2 diabetes have a higher incidence of LFT and KFT abnormalities than individuals who do not have diabetes so that all the parameters of LFT and KFT were evaluated to check the efficacy and safety of the test drugs. Values of LFT (SGOT, SGPT and ALP) and KFT (Serum Urea, Serum Creatinine and Serum total protein) at the end of the study significantly reduced in test group of SZ-I LD, SZ-I HD, SZ-II LD and Hummaz LD with respect of negative control while the all parameters were to be found prominently decreased in test group

of SZ-II HD, Hummaz HD and Standard drug with respect to the negative control which is highly significant ($P<0.001$ vs negative control).

Body weight of the animals was also recorded to determine the effect of diabetes on the body weight. The animals who received HFD plus low dose of STZ only showed a significant fall in their body weight, while the animals treated with standard drug did not show any reduction in the weight at the end of study, rather they show a significant increase.

Urine sugar was found to be present only in diabetic control group while other groups did not show its presence. This result strongly conform the findings of other parameters and suggests that test drugs possess significant hypoglycemic effect.

Histopathological study was investigated in the liver, kidney and pancreatic tissues sections of animals. Pathological lesions were evoked in cells of diabetic rats. The oral administration of SZ-II HD, Hummaz HD and standard drug at a dose of 800 mg, 500 mg and 40 mg/ kg body weight respectively have more efficacy than the low dose of SZ-I LD, SZ-II LD, Hummaz LD and SZ-I HD. The results indicate the extract exhibit the protective effect on tissues and prove its potential as a hypoglycemic agent.