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Synergistic effect of grape seed extract in combination with green coffee bean for the treatment of diabetes mellitus

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Abstract

The proposed project successful attempt has been made to synergistic effect of grape seed extract in combination with green coffee bean for the treatment of diabetes mellitus. I started process plant extraction is a modern technique that offers a rapid method for extraction phytoconstituents. Coffee arabica extract percentage yield 11.44% and grape seed extract percentage yield 10.23% mixture of these two extract were taken 1:1 ratio for the present study to find the synergistic anti diabetic activity phytochemical study conducted to investigate the present various components CBGSC and process of Alpha-Amylase inhibition activity extract lower that the standard acarbose[IC50=9.08µg/ml]grape seed extract was used alone AAI rate 24.20ug/ml and green coffee extract AAI-rate 20.13µg/ml combination of extract observed at 92.56%at360ug/ml IC50 was found to be 17.33µg/ml. alpha-glucosidase inhibition GS extract concentration 88.72% AGE.IC50 value 17.04µg/ml. GC Extract concentration 89.61%AGE.IC50 value 15.42µg/ml. Molecular docking analysis was conducted human alpha glucosidase binding energy and beta -D-glucopyranosyl binding energy 9.39Kcal/mol . and inhibition constant 130.88nm. Binding site of ligand hydroxyl group of Ligand - binding distance LLN167o-H-o -3.2, ASP199O-H-o-3.1, ASG411N-H-o-2.6 All the process are followed by as per WHO and ICH guidelines

Keywords: AAI-ALPHA AMYLASE INHIBITION; CBGSC-COFFEE BEEN GRAPE SEED EXTRACT; AGE-ALPHA GLUCOSIDE ENZYME INHIBITOR

1. Introduction

Traditional medicine is an ancient healing practice that predates the advent of modern health science. Herbal remedies derived from natural sources offer an alternative to synthetic drugs and have gained significant interest in health care systems. Currently, over 90% of therapeutic drugs are derived from natural sources and a substantial portion of the global population relies on herbal remedies for their primary health care needs. Diabetes mellitus is characterized by insufficient levels of blood insulin resulting in hyperglycemia due to reduce sensitivity of receptors decreased insulin secretion and pancreatic cell dysfunction. This disruption in normal sugar regulation leads to increased blood sugar level. Insulin plays a crucial role in utilizing glucose for energy and helps restore sugar level with in the normal Range . Hyperglycemia is primarily caused by increased hepatic glucose output in the presence of hyperinsulinemia .According to a 2014 survey by the WHO,422 million individuals world wide had a diabetes mellitus. In india alone 62 million people are affected by diabetes .they are types of diabetes namely diabetes mellitus I and diabetes mellitus II with the latter affecting approximately 90% of the population .Diabetes mellitus can lead to complication such as renal failure, blindness, impotence, cerebrovascular, disorders and cardio vascular disorders. Herbal products have been utilized in the treatment of diabetes mellitus and its associated complications due to the presence of phytoconstituents that can help reduce glucose and cholesterol levels .Ancient literature mentions the use of herbal plants for managing diabetes mellitus. The isolation of phytoconstituents with enhanced therapeutic effects for various aliments field of herbal

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medicine. WHO has acknowledged the effectiveness of phytochemicals in reducing blood glucose levels and potential use as anti diabetic agents. Literature survey regarding the plants having ethnobotanical information. selection and collection of plants materials,extraction of soluble components from the present part of the plant of the plant by the using solvents. phytochemical analysis and identification of active compounds from the plant extracts. Performing biological assay by using suitable anti diabetic assay model. Molecular docking studies of active compounds from plant extracts.

1.1. Plant profile

Kingdom -plantae,Clade – tracheophytes,angiosperms,eudicots Species - Coffea arabica, Order- Gentianales, family-rubiaceae and Genes – coffea. Species- Vitis vinifera Order – vitals, Family- Vitaceae,Genes – Vitis. The present work aims to screen the synergistic effect of grape seed extract and green coffee extract for the antidiabetic activity.

2. Materials and method

2.1. Extraction of plant

2.1.1. Microwave assisted extraction (MAE)

Plant material 10g of seed powder solvent used methanol and microwave oven CATA-R operating at 800 W temperature extraction carried out 50·c performed period of time 5 minutes. After filtration process to remove solid particles or impurities. the filter obtained evaporated concentration used rotary flash evaporator obtain dry extracts calculate the percentage yield determined by comparing the weight of the dry extract obtained initial weight green coffee extract coffea arabica used percentage yield 11.44% and grape seed percentage yield 10.23%. Mixture of these two extracts were taken 1:1 ratio for the present study to field the synergistic diabetic activity Qualitative phytochemical analysis test for alkaloids, saponin, tannins, cardio glycoside, flavonoids,phenols, steroids, terpenoids, quinones, proteins .

Alpha-Amylase Inhibition Assay (AAI)

The a-Amylase inhibitory activity of the test samples (CBGSE) was carried out the standard method with minor modification 100ulof a a-amylase 0.1µg/ml was mixed with different concentration of test samples,Refence standard (Acarbose) and control and pre – incubated at37·c for 15 min 100ul of starch solution was added to initiate reaction incubation was done 37·c for 60 minutes . the absorbance of the activity was measured at 565nm . inhibitory activity formula

$$\%\text{Inhibition} = [(\text{OD of the test} - \text{OD of the control}) / \text{OD of test}] \times 100$$

Inhibitory activity of the extracts standard acarbose grape seed extract a-amylase inhibition rate 24.20µg/ml and green coffee extract inhibition rate was 20.13µg/ml. Combination of extracts has inhibition activity was observed at 92.56% at 360µg/ml and the IC 50was found to be 17.33µg/ml. More results details refer form graph no:1

Alpha-Glucoside Inhibitory Activity

a-glucoside inhibitory activity was measured using p- nitrophenyl a-D- glucopyranoside as the substrate prepared in 2.02M phosphate buffer PH6.3 the enzyme solution 0.13ml was incubated with extract 0.13ml and 0.02M phosphate buffer 0.45ml for 1hour at 250·c .after pre incubation 2M p- nitrophenyl a-D- glucopyroanoside 0.67ml mixture was incubated for another 30 minutes at 300 ·c .Determination of the amount p-nitro phenol formed was read spectrophotometrically at 405nm . The inhibition activity calculation as [(Ao-Ae)/Ao] ×100

grape seed extract concentration 88.72% alpha glycoside enzyme with an IC 50value 17.04µg/ml. green coffee extract concentration of 89.61% AGE inhibitory activity IC50of 15.42µg/ml. Combination of extracts 1:1 radio demonstrated an IC50 value of13.01µg/ ml .More result details refer from graph no:2

3. Result and discussion

3.1. Preparation of ligand for docking analysis

All the ligands or molecules involved in our study were collected from the available literature all the molecular structure were reproduced in ultra – version 2010 and then all ligands were saved in molecular format with MOE after structure preparation and these were protonate 3D at a temp of 3000·c PH7 .The MMFF94 force filed was used with no periodicity and the constraints were maintained at the rigid water molecule level.

3.2. Preparation of protein and molecular docking

Molecular docking studies were performed to investigate the binding mode between the compound ellagic acid pentoside, kaempferol rutinoside, Isorhamnetin -3-o-glucoside 3-o-beta- D- glucosidease was 3D protonated and then energy minimization was performed using MOE software. Protein-ligand docking score, ligand properties, and 2D&3D structures were saved . the best scoring poses as judged by the vina docking score were chosen and visually analyzed using pyMOL1.7.63software .

3.3. Molecular docking studies

The molecular docking studies was conducted to investigate the structural interaction between the identification metabolites and the α-glucoside active site and inhibition by secondary metabolites of plant has been widely adopted. This hydrogen bond interaction and the binding site contribute to their inhibitory activity against the alpha – glucoside enzyme the diagram demonstrated that the ligand were deeply embedded in the active pocket of the enzyme. Over all docking studies provided insights into the alpha-glycosidase inhibition mechanism and confirmed the anti diabetic potential of the plant extract by revealing the specific bonding potential of the plant extract by revealing the specific bonding types between the protein and phytochemicals over all docking result of the ligands human alpha glucosidase PDBID :5ZCD below the table no :1

Table 1 Over all docking results of the ligands

Compound Id & Figure .No	Binding energy (kcal/mol)	inhibition constant	Hydrogen bond	bonding distance	Binding site of ligand
Ellagic Acid Pentoside Figure.No:3	-6.58	15.02µM	THR409(O)-H-O GLN256(N)-H-O ASP199(O)-H-O ARG411(N)-H-O	2.7 3.3 2.4. 3.1	Hydroxyl Group Of Ligand
Kaempferol Rutinoside Figure.No:4	-6.86	9.32µM	ASN258(N)-H-O ASN258(N)-H-O ASP327(O)-H-O	2.7 3.1 2.6	Hydroxylgroup Of Ligand
Isorhamnetin-3-O-Glucoside Figure.No:5	-12.39	827.92pM	HIS203(N)-H-O PHE282(O)-H-O MET285(O)-H-O ASP382(O)-H-O ASP327(O)-H-O GLN256(N)-H-O	2.8 2.8 3.2 2.7 2.7 2.8	HYDROXYL GROUP OF LIGAND
3-O-Beta-D-Glucopyranosyl-Stigmasterol	-9.39	130.88nM	GLN167(O)-H-O ASP199(O)-H-O ARG411(N)-H-O	3.2 3.1 2.6	HYDROXYL GROUP OF LIGAND

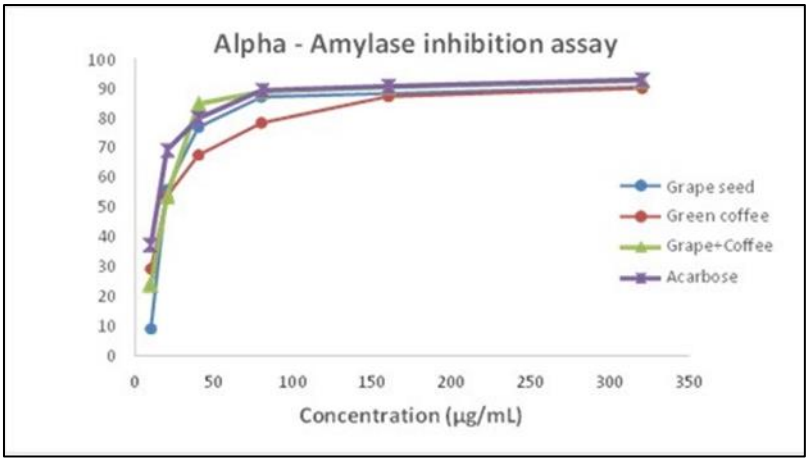

Figure 1 Alpha – amylase inhibition assay

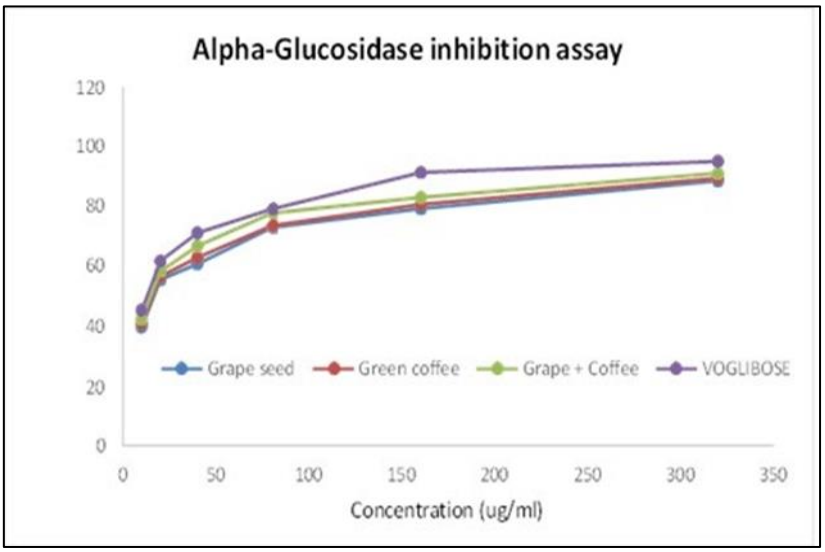

Figure 2 Alpha- glucoside inhibition assay

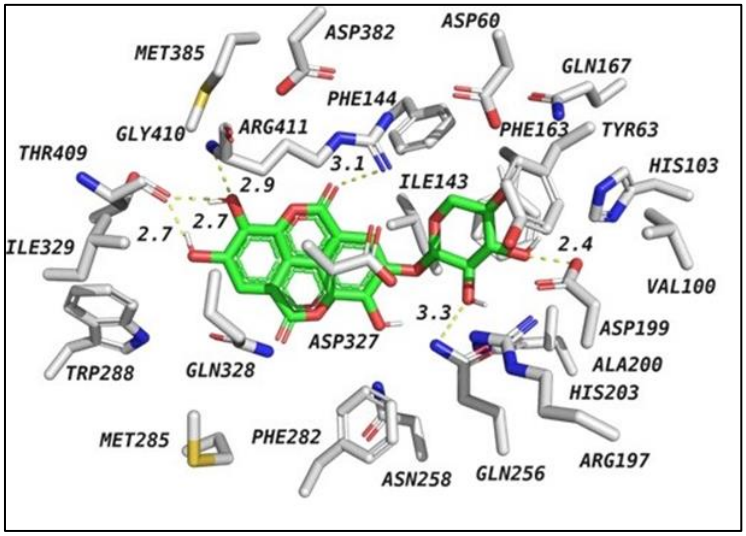

Figure 3 3-D interaction pattern of human alpha glucoside and ellagic acid pentoside

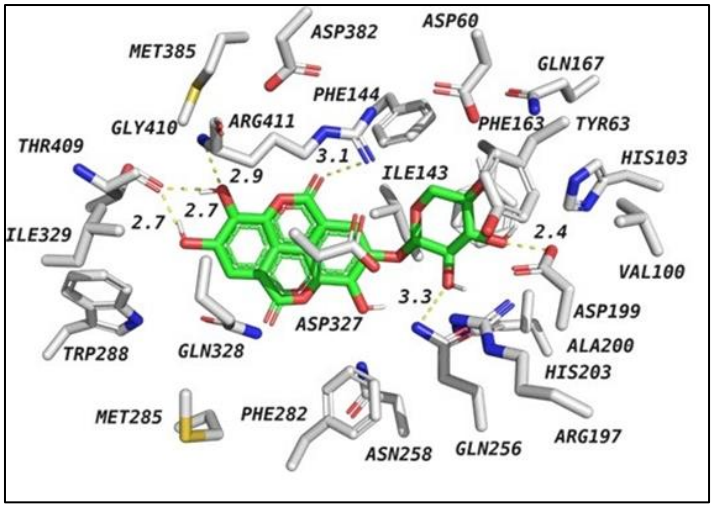

Figure 4 3-d interaction pattern of human alpha glucoside and kaempferol rutinoside

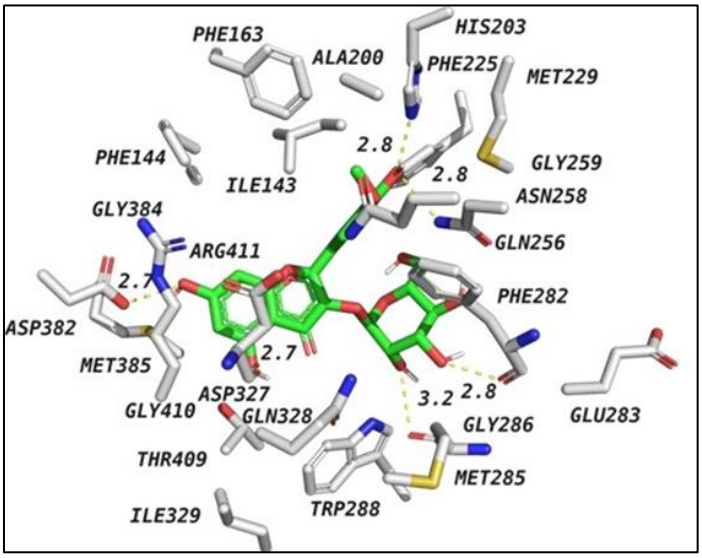

Figure 5 3-dinteraction pattern of human alpha glucosidase and isorhamnetin-3-o-glucoside

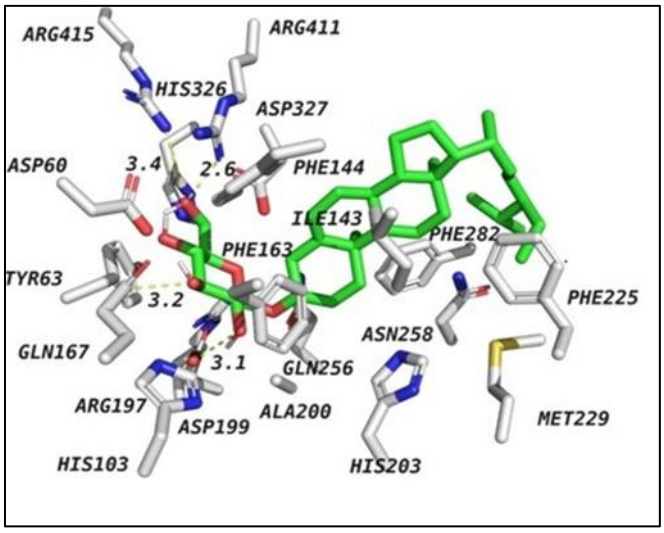

Figure 6 3-d interaction pattern of human alpha glucosidase and 3-o-beta-d-glucopyranosyl-stig

4. Conclusion

The analysis of medicinal plants involves extracting bioactive compounds using appropriate solvents based on the targeted compounds of interest. Combination grape seed extract and green coffee extract showed synergistic effect against alpha – amylase and alpha – glucosidase enzyme. These herbal combination can be used to control postprandial hyperglycemia and can also afford the antidiabetic activity to patients with T2DM.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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