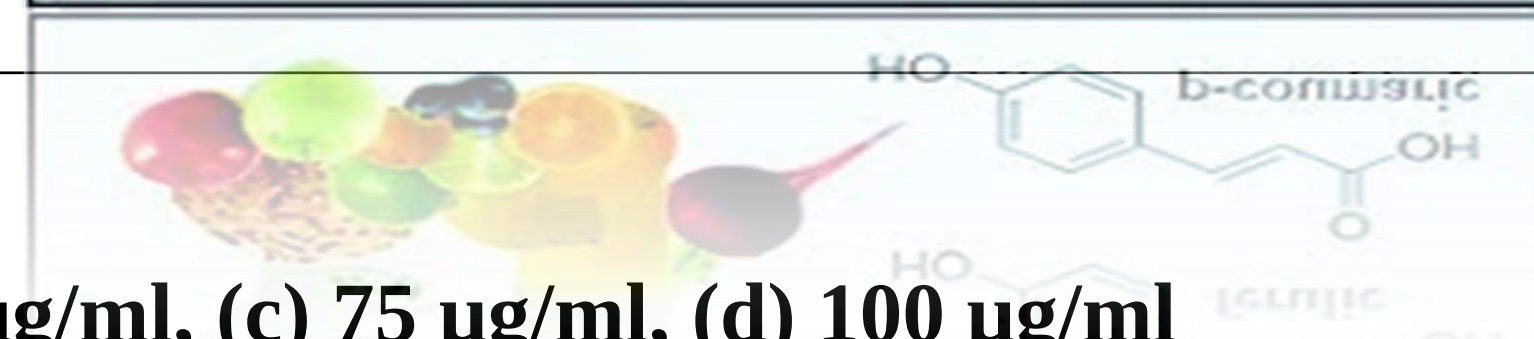


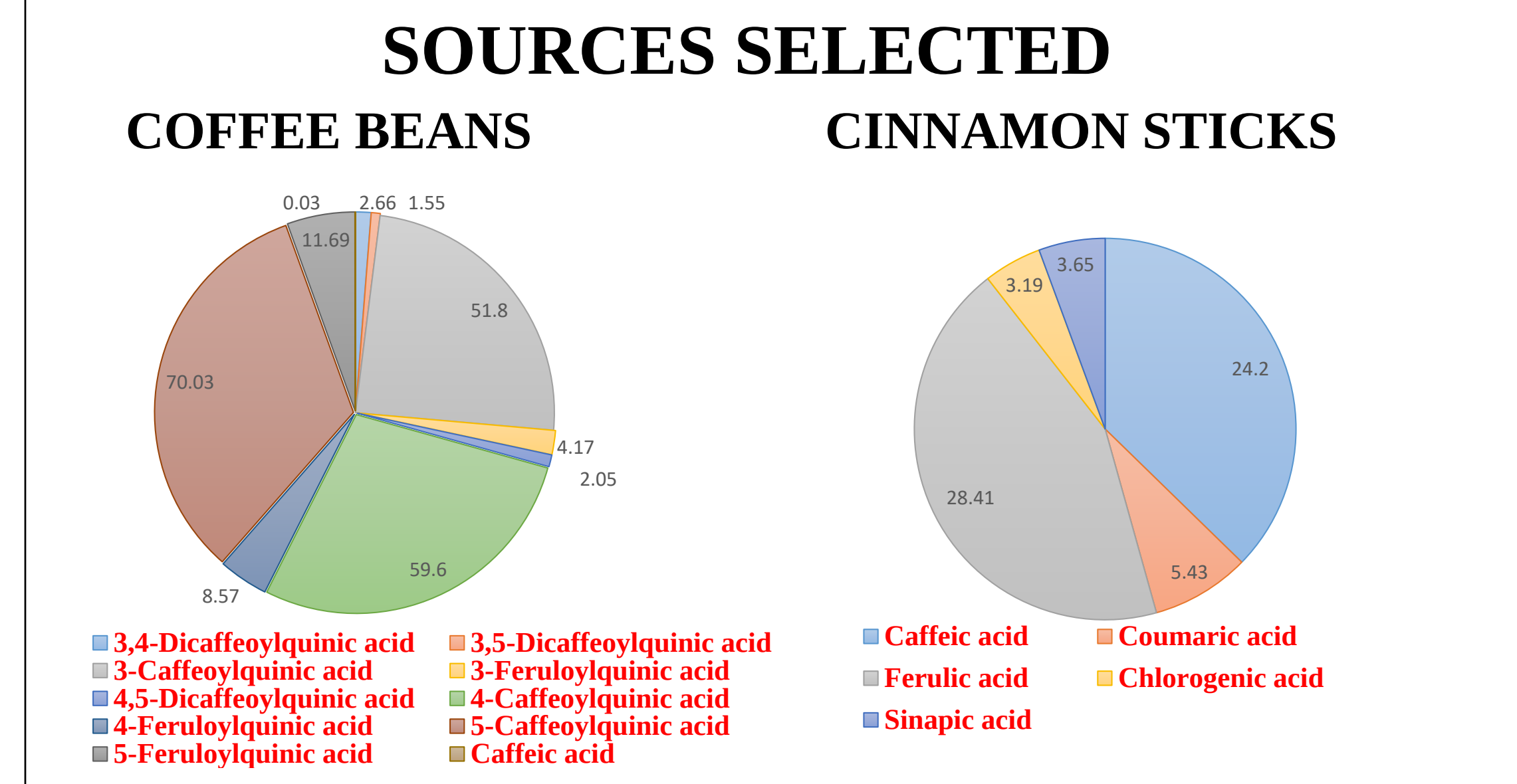


Abstract: With increasing concern around the use of synthetic compounds as therapeutic agents, the pharmaceutical sector of nutraceuticals has grown popular and continues to be a field of interest and constant research [1,2] . This sector ensures the use of natural food resources for the prevention and treatment of diseases. For present study natural derivatives of Hydroxycinnamic acids were considered which are biologically active compounds, synthesized as secondary metabolites in plants. These compounds and their derivatives are shown to exert anti-oxidant, anticollagenase, anti-inflammatory, anti-microbial, anti-tyrosinase, UV protective effects, anti-aging, anti-carcinogenic, anti-proliferative, and anti-hyperlipidemia activities [3] . The current work includes the extraction, identification of phenolic compounds, in-silico based modelling [4–6] and in vitro evaluations. The extracts of two food sources were sed for in vitro analysis to assert the activities in question. Biochemical profiling demonstrated; Phenolic content in methanolic extract as 80.11 mg/ml and 93.25 mg/ml respectively, while hydroxycinnamic acid derivative content was scored to be 7.47 mg/ml and 5.32 mg/ml. The purity of the derivatives extracted was evaluated using chromatographic technique, wherein only one single spot was observed for each extract. The cytotoxicity of the extracts was studied on blood cells and MCF-7 breast cancer cell line and IC 50 values 60.04 µg/ml, 81.12 µg/ml and 51.14 µg/ml, with 95% of confidence level or profile likelihood. In-silico including molecular-docking studies using caffeic acid, chlorogenic acid, ferulic acid and rosmarinic acid as ligands and interactions study was carried out with receptor peroxisome proliferator activated receptor- γ, proteins tumor-necrosis factor- α and interleukin-6, receptors vascular endothelial growth factor receptors. All the results from molecular docking exhibited a good docking score of all selected ligands caffeic acid, chlorogenic acid, ferulic acid and rosmarinic acid with specific target by occupying within the binding site region. The anti-inflammatory and anti-obesity activities were confirmed using CRP and glucose content tests carried out by Clinical partner, which further assert that these derivatives are promising natural therapeutic agents.

Keywords: Hydroxycinnamic acids, Cancer, Inflammation, Obesity

Background: POLYPHENOLS - Bioactive micronutrients obtained from plant foods and plant-derived beverages HYDROXYCINNAMIC ACIDS - Non-essential nutrients, which form the largest class of phenolic compounds

Natural Sources		Health Benefits	
Ripe fruits	Tea	Anti-Inflammatory	Anti-Cancer
Vegetables	Coffee	Anti-Oxidant	Anti-Microbial
Spices	Wine	Anti-Tyrosinases	Anti-Aging
Cereals	Oils	Anti-Proliferative	Anti-Hyperlipidemic
Herbs	Nuts		



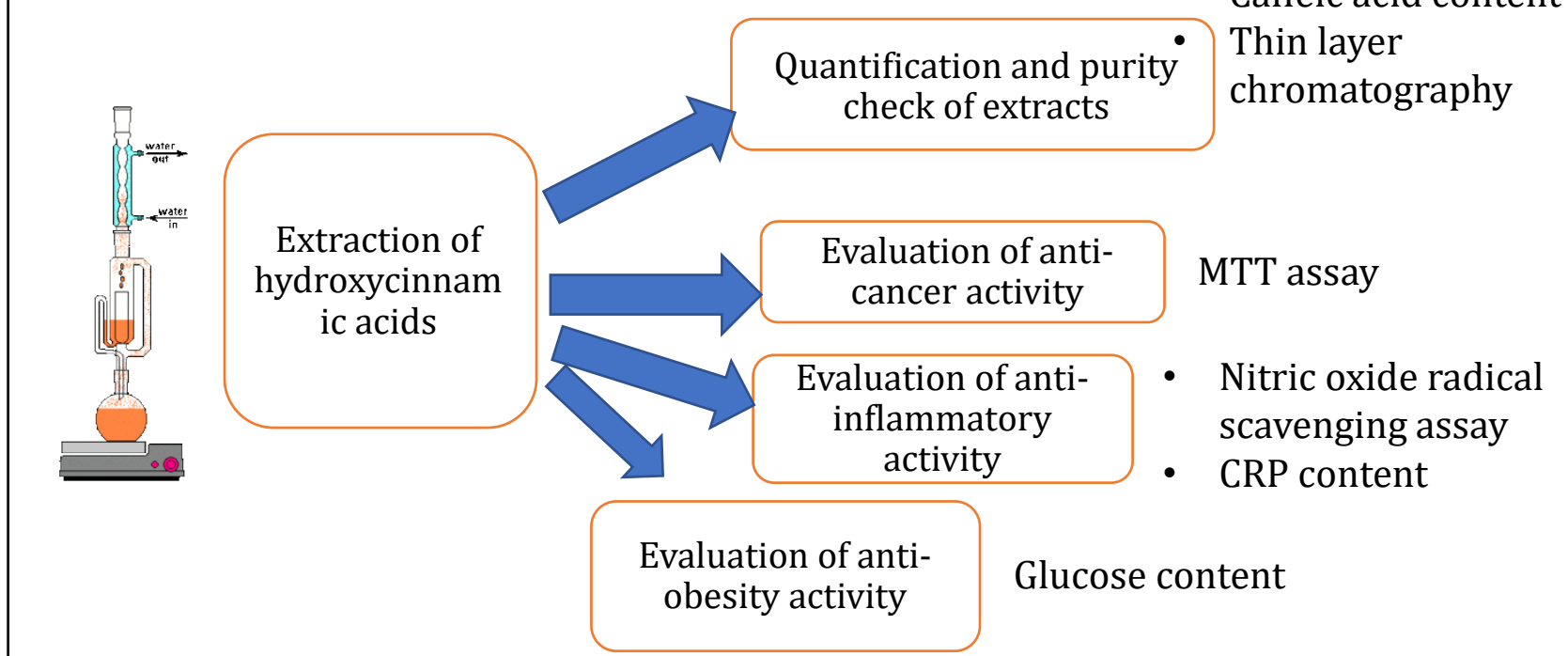
Objective: Identification of food resources rich in HCAs Extraction of HCAs from identified food resources

In silico ADMET analysis and Interaction study *In vitro* toxicity analysis

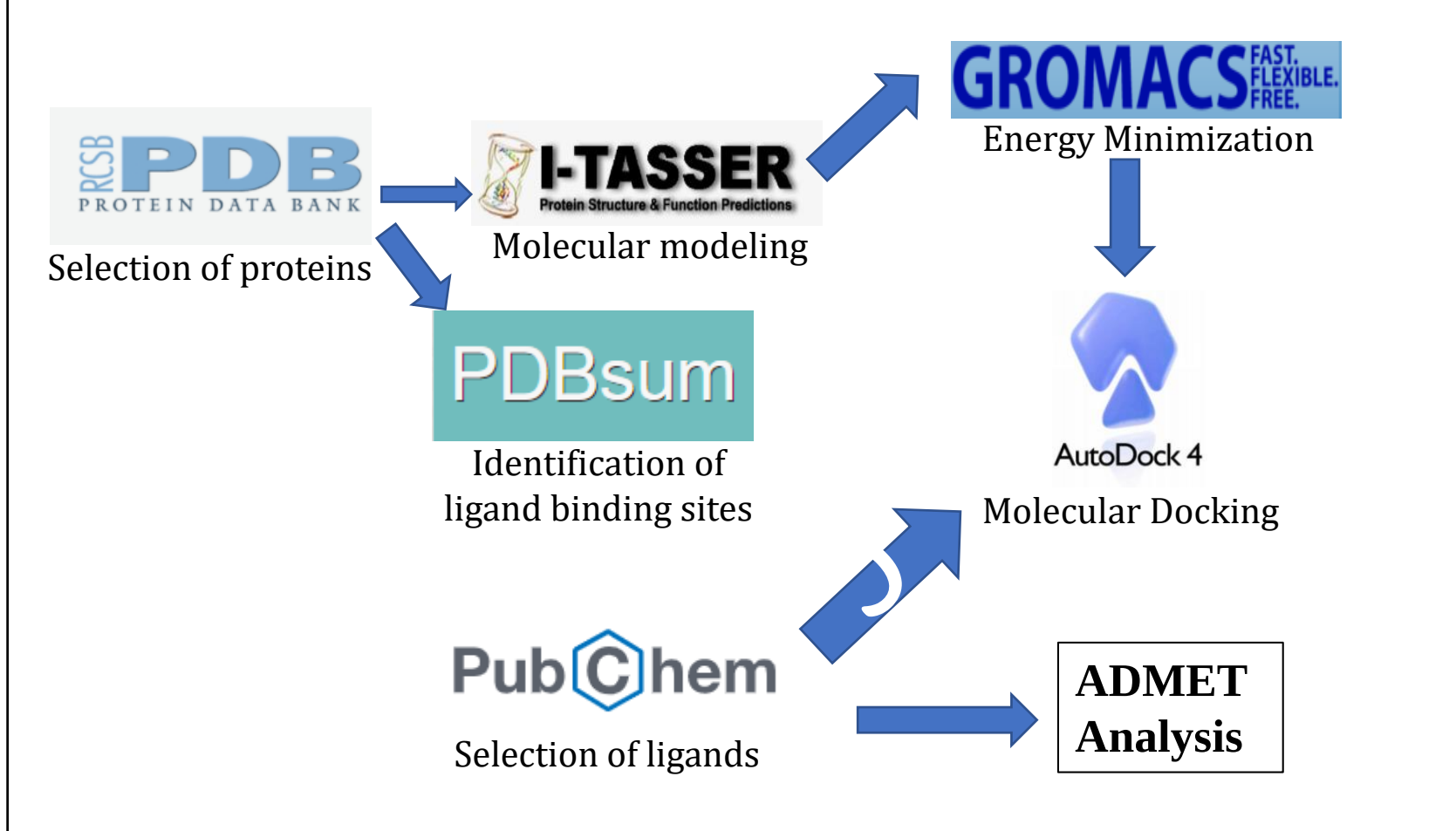
Evaluation of anti-cancer activity of HCAs on MCF-7 cells

Data Set	Receptors	Ligands
PPAR-γ	IL-6	Caffeic acid
TNF-α	VEGFR-1	Chlorogenic acid
VEGFR-2		Coumaric acid
		Ferulic acid
		Rosmarinic acid

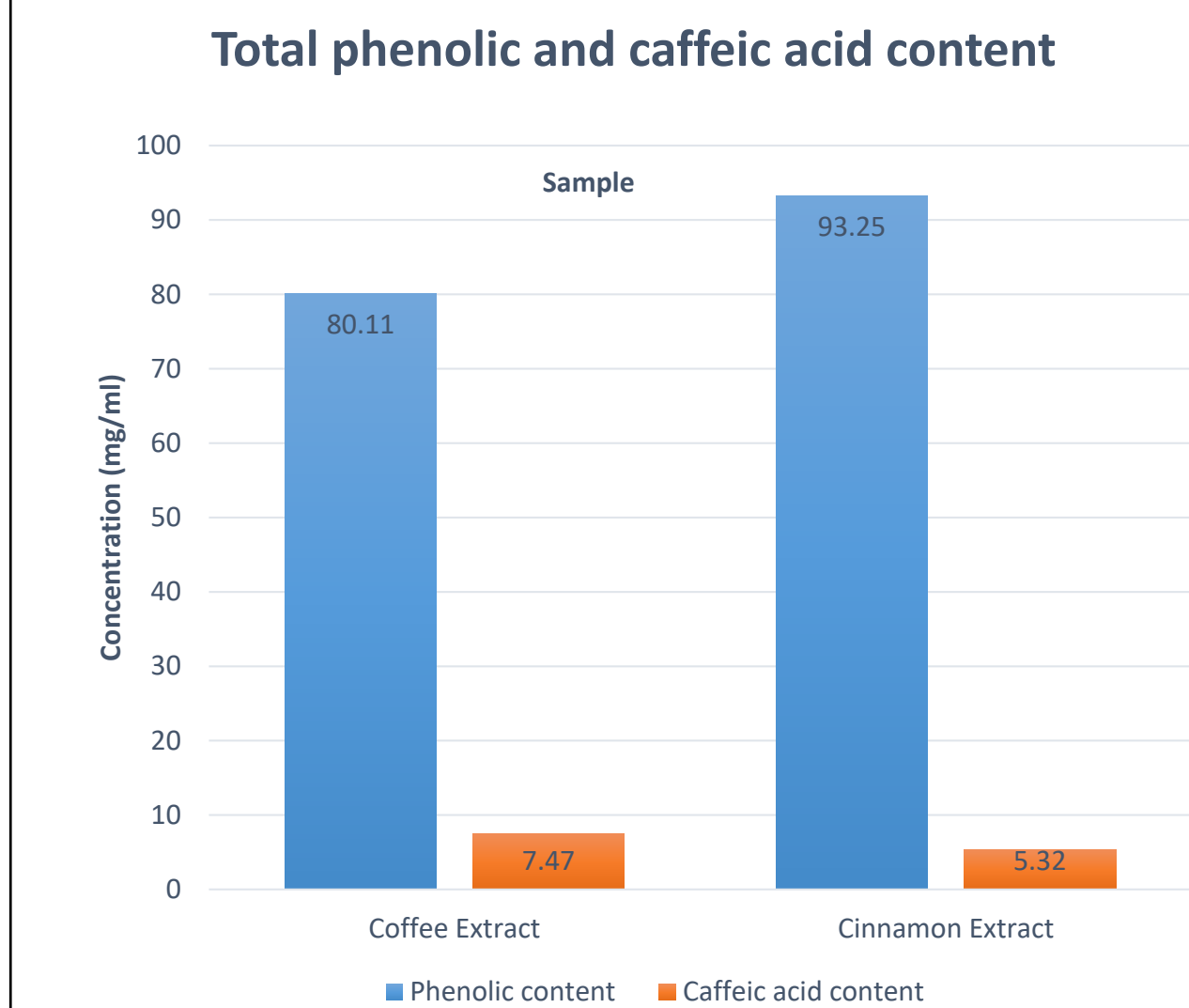
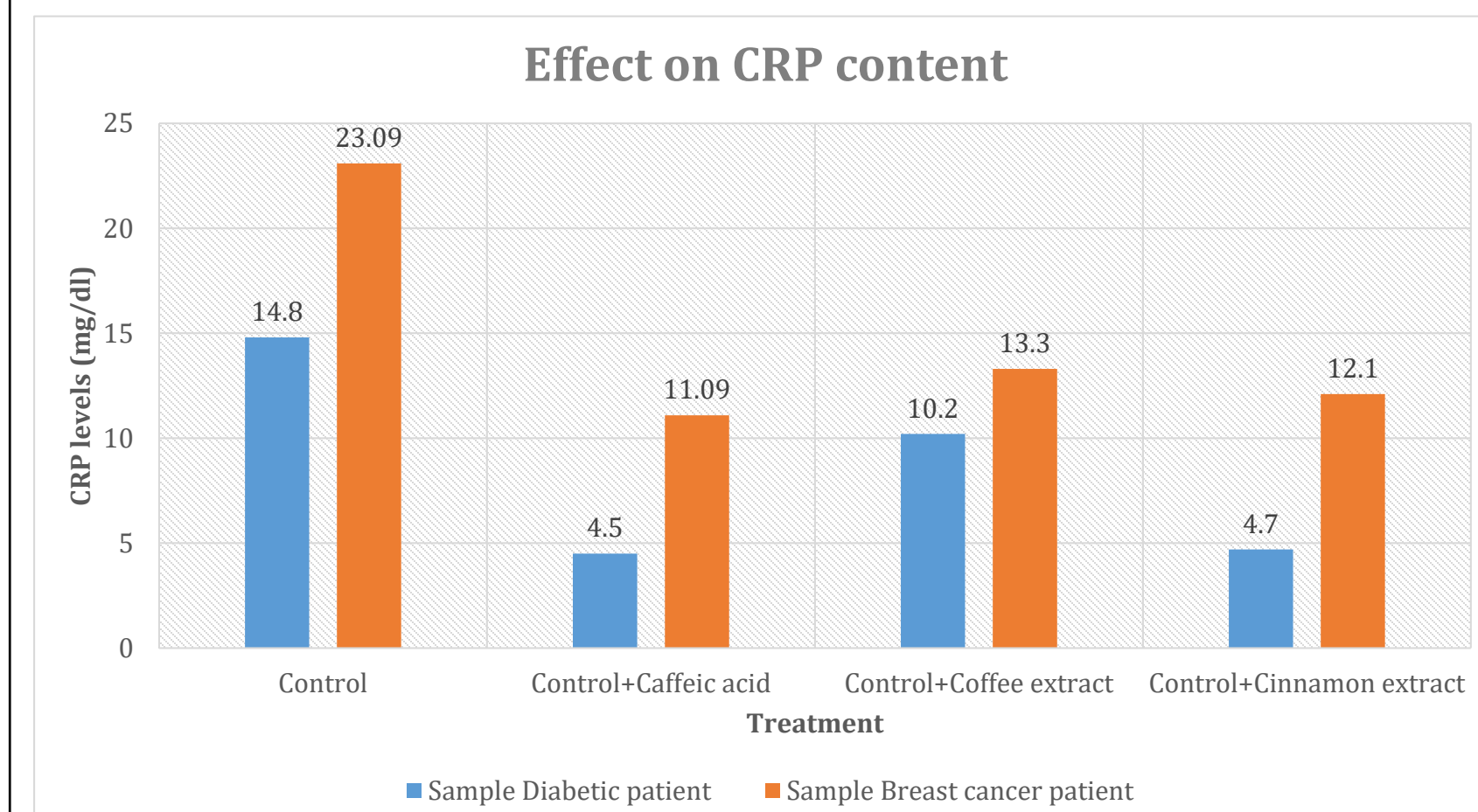
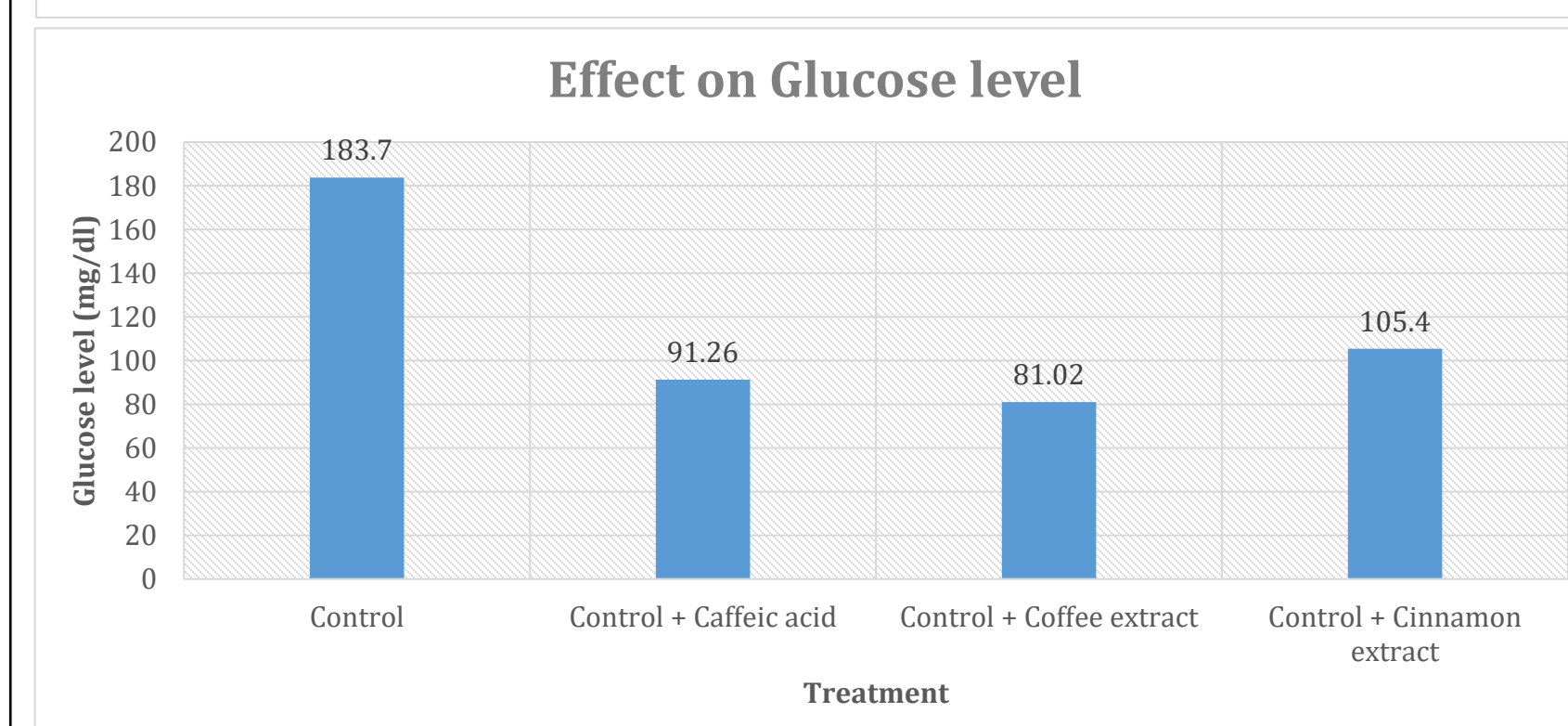
Methodology: *IN VITRO STUDIES*



IN SILICO STUDIES



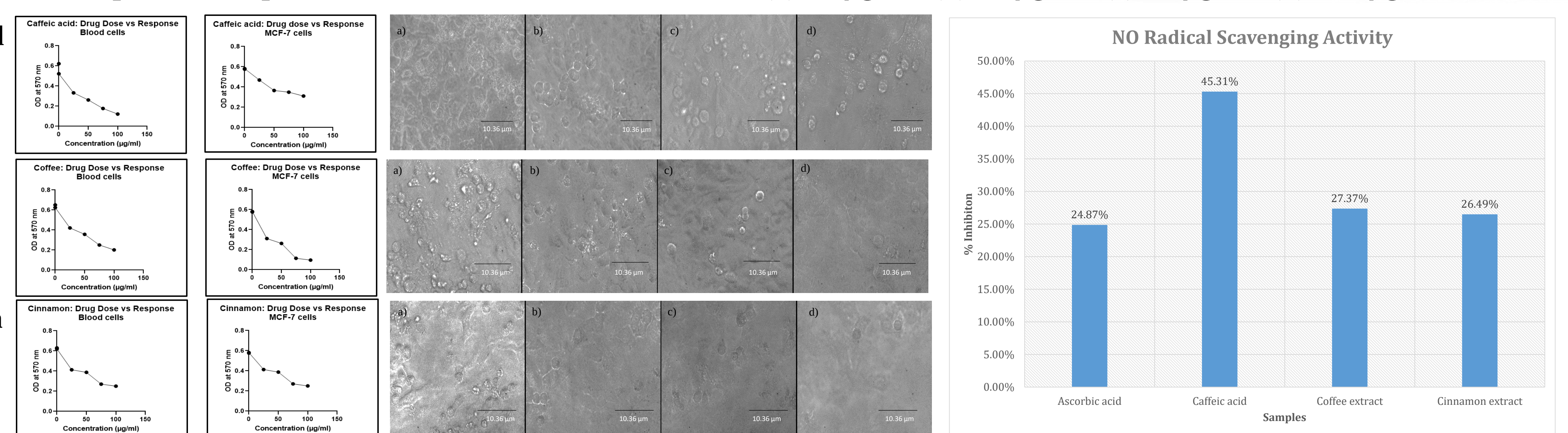
Results:



ADMET Analysis	Caffeic Acid	Chlorogenic Acid	Coumaric Acid	Ferulic Acid	Rosmarinic Acid
Formula	C9H8O4	C16H18O9	C9H8O3	C10H10O4	C18H16O8
Molecular Weight	180.16 g/mol	354.31 g/mol	164.16 g/mol	194.18 g/mol	360.31 g/mol
#heavy atoms	13	25	12	14	26
#aromatic heavy atoms	6	6	6	6	12
#rotatable bonds	2	5	2	3	7
#H bond acceptors	4	9	3	4	8
#H bond donors	3	6	2	2	5
ESOL class	very soluble	very soluble	soluble	soluble	moderately soluble
Lipinski #violations	0	1	0	0	0
Bioavailability score	0.56	0.11	0.85	0.85	0.56
Synthetic accessibility	1.81	4.16	1.61	1.93	3.38
Ames mutagenesis	-	-	-	-	-
Acute Oral Toxicity (c)	IV	III	III	IV	III
Carcinogenicity (binary)	-	-	-	-	-
Human Intestinal Absorption	+	+	+	+	+
Plasma protein binding	0.78702253	0.81075615	0.72038084	0.92533582	1.0009712
Water solubility	-1.6939286	-2.4571991	-2.2239704	-2.476627	-3.2050309

CYTOTOXICITY ACTIVITY

Dose dependent response on Blood cells & of MCF cells at (a) 25 µg/ml, (b) 50 µg/ml, (c) 75 µg/ml, (d) 100 µg/ml



Molecular docking	Reference Molecule	Caffeic acid	Chlorogenic acid	Coumaric acid	Ferulic acid	Rosmarinic cid
PPAR-γ						
IL6						
TNF- α						
VEGFR-1						
VEGFR-2						

Conclusion: The phenolic acid content in coffee and cinnamon extract were found to be 80.11 mg/ml and 93.25 mg/ml respectively, while the caffeic acid content was found to be 7.47 mg/ml and 5.32 mg/ml respectively. From in vitro cytotoxicity assay, IC50 was calculated to be 51.14 µg/ml for caffeic acid, 64.04 µg/ml for coffee extract and 81.12 µg/ml. From tests conducted in Seven Star Pathology Lab, the extracts were shown to be effective in reducing CRP and glucose content. *In silico* studies showed effective interactions of different HCAs with receptors/proteins involved in key pathways of the targeted therapeutic areas.

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