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Anti-inflammatory, antidiabetic and hypolipidemic potential of *Cinnamomum verum* J. Presi bark coupled with FT-IR and HPLC analysis

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Abstract: Medicinal plants and herbs are used from ancient times for the treatment of acute or chronic diseases because they are easily accessible and have low cost. In this research, we investigated anti-inflammatory, hypoglycemic and hypolipidemic potential of ethanolic extract of *Cinnamomun verum* J. Presi bark. Anti-inflammatory activities were performed by proteinase inhibition, heat-induced hemolysis and BSA denaturation. Advance glycation inhibition potential was performed by β-amyloid formation, fructosamine assay and free carbonyl group estimation. The in-vivo antidiabetic and anti-obesity potential were evaluated by using high-fat, high-sugar diet (HFHSD) model. FT-IR and HPLC were also performed. Results showed that proteinase showed 76±1.06%, heat-induced hemolysis showed 59±1.02% and BSA denaturation showed 48.2±1.04% inhibition. The β-amyloid formation assay showed an absorption of 0.022, the fructosamine assay showed 33.3±0.04% and free carbonyl group estimation showed 20.3±0.02% inhibition. The in-vivo study showed that ethanolic extract significantly improves body weight, blood glucose level, lipid profile and liver markers in a dose-dependent manner. The FT-IR spectrum confirmed the presence of multiple functional groups, while HPLC identified thymoquinone, coumarin α-cysteine. It is concluded from these results that *Cinnamomum verum* J. Presi bark ethanolic extract can be used to treat inflammation, hyperlipidemia and diabetes.

Keywords: Obesity, atorvastatin, glibenclamide, cinnamomum and inflammation.

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INTRODUCTION

Economic growth and globalization have led to lifestyle changes characterized by increased consumption of unhealthy foods and reduced physical activity, significantly contributing to the global obesity pandemic, particularly in developing countries (Ariyanto *et al*., 2021). Many long-lasting diseases, like diabetes, tumors, neurodegenerative disorders and heart-related diseases, are exacerbated by oxidative stress (Mwalimu and Packirisamy, 2023). Chemicals, physical, and microbial agents increased oxidative stress and induce damage to the cellular structure, potentially destroy tissues and leads to inflammation (Ramos-González *et al*., 2021). The inflammation is directly correlated with exceeding weight and is dominated by an imbalance between pro- and anti-inflammatory processes, abnormal cytokine levels and exaggerated production of C-reactive protein. Long term use of over-nutrition leads to systemic toxicity produces by glucose and unoxidized long-chain fatty acids and can stimulate the synthesis of pro-inflammatory adipokines. High-fat diet (HFD) feeding can cause imbalances in the adipose tissue environment and alter its anti-inflammatory state by recruiting pro-inflammatory immune cells (Savulescu-Fiedler *et al*., 2024). Systemic inflammation is a key contributor to the onset and progression of several obesity-associated diseases like dyslipidemia, characterized by high triglycerides and LDL-c, along with low HDL-c, significantly contributes metabolic syndrome like type 2 diabetes, cardiovascular disease and cancer, indirectly lowering the quality of life (Oh *et al*., 2023). This condition is associated with dysregulated adipocyte differentiation due to an unbalanced metabolic flux, where energy storage surpasses energy expenditure, and is influenced by genetic, endocrine, and neurological factors (Ezenwaka *et al*., 2014). Chronic unbalanced metabolic activity increases the likelihood of comorbidities, making prolonged weight gain from fat accumulation in adipose tissue harmful to health (Kim *et al*., 2022). Oxidative stress, triggered by elevated free radicals and reactive oxygen species, plays key role in the development of diabetes miletus. Type 2 diabetes, a metabolic disorder in which either insufficient insulin is generated by the pancreas or produced insulin is ineffective to control blood sugar levels. More than 80% of people worldwide utilize conventional herbs to treat a range of ailments and disorders. Medicinal plants containing antioxidants, flavonoids, alkaloids, carotenoids, vitamins, glycosides and terpenoids can both reduce oxidative stress and regulate blood glucose level (Mwalimu and Packirisamy, 2023, Khizar *et al*., 2019). Phytoconstituents such as

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phenol, alkaloids, flavonoids, glycosides, tannins and steroids are the prime suspects in cell division, growth, reproduction, respiration, metabolism and storage (Sutariya *et al*., 2023). Medicinal plants with high phenolic contents have potent radical scavenging, anti - carcinogenic characteristics, anti-inflammatory, pro-apoptotic, anti-angiogenic, anti-epileptic effects, anti-obesity activities, inhibit low-density lipoprotein oxidation, reduce the progression of chronic and acute diseases such as cardiovascular and neurological disease (Sutariya *et al*., 2023, Lamichhane *et al*., 2023). The literature shows that several plants, such as *Vitis vinifera*, *Cinnamomum verum*, *Streblus asper* and *Sida cordifolia*, contain a range of polyphenols, with diverse bioactivities (Lamichhane *et al*., 2023).

Cinnamomum verum or Ceylon cinnamon is native to Sri Lanka, belongs to Lauraceae family, small evergreen tree, primarily used in cuisine as a condiment and flavoring agent and has long been employed in traditional folk medicine. It exhibits a range of significant biological activities, including antidiabetic, anti-obesity, antipyretic, antilipemic, antiviral, antifungal, gastroprotective, antiulcerogenic antitumor, antimicrobial, antiallergic, antihypertensive and immunomodulatory effects (Gulcin *et al*., 2019). Cinnamon extracts contain flavonoids, phenols, alkaloids, quinones, steroids, saponins, tannins, procyanidins, catechins, cinnamaldehyde, cinnamic acid, eugenol and coumarin (Gupta Jain *et al*., 2017). However, beside of all these therapeutic uses, there is a need of strong rationale to validate the hypoglycemic, anti-inflammatory and hypolipidemic effect of cinnamon. Therefore, the present study aims to determine the anti-inflammatory, anti-glycation and anti-obesity potential alongside HPLC and FT-IR analysis for phytochemical profiling.

MATERIALS AND METHODS

Collection of plant material

Bark of *Cinnamomum verum* J. Presi (1.0kg) was obtained from a local market in Sahiwal, Punjab, Pakistan. The crude drug was authenticated by Professor Dr. Zafarullah Zafar from the Department of Botany at Bahauddin Zakariya University, Multan. For future reference a small sample was kept in the herbarium of the Department of Pharmacognosy, Faculty of Pharmacy, Bahauddin Zakariya University, Multan, Pakistan, under specimen voucher number (www.theplantlist.org/tpl1.1/record/kew-2721692). The bark then grinded to produce a coarse powder.

Extract preparation

Five hundred grams of coarsely ground *Cinnamomum verum* J. Presi bark (CvB) powder was macerated in 1.5 liters of 98% ethanol for seven days, with occasional shaking. The soaked material was filtered using Whatman filter paper. The solid residue remaining after the first filtration was macerated again twice, first in 1.0 liter and then in 0.8 liter of 98% ethanol, and the filtrate was collected each time. All three filtrates were then combined and dried using a rotary evaporator (Buchi, Switzerland) under a pressure of 74.51 torr, at 4 rpm, and a temperature range of 30 to 40ºC. The resulting thick, viscous plant extract paste was weighed to determine the percentage yield and stored in an airtight container.

Anti-inflammatory activity

Proteinase Inhibition activity

The experiment was conducted following a modified procedure from *Sakat et al*. (2014). The reactants (2 mL) consist of 1 mL of CvB at a concentration of 66 µg/mL 1 mL of 20 mM Tris HCl buffer (pH 7.4), and 0.06 mg of trypsin. The chemical blend was incubated at 37℃ for 5 minutes before adding 1 mL of 0.8% w/v casein. This was followed by an additional 20-minute incubation. Subsequently, 70% perchloric acid (2 mL) and the opaque sample was then centrifuged, and the clear phase was collected. The absorbance of the clear liquid phase was determined at 210 nm using a UV/VIS spectrometer (Optima, SP-3000, Tokyo, Japan), with the buffer used as a reference (Sakat *et al*., 2010). The experiment was conducted thrice and % proteinase inhibition was calculated using Eq. 1 and the outcomes are mentioned in table 1.

$$\% \text{ Proteinase Inhibition} = \frac{A_c - A_s}{A_c} \times 100 \quad \text{…….. (Eq. 1)}$$

Absorbance of Control = A_c, Absorbance of Sample = A_s

Heat induced hemolysis

The test was executed using a modified method of *Gunathilake et al.* 2018. In summary, blood cell suspension (0.05mL) was combined with 41.6µg/mL CvB (0.05mL) in distilled water, followed by mixing with 7.4 pH phosphate buffer (2.95mL). The mixture underwent incubation at 54°C for 20 minutes in a shaking water bath. Post-incubation, the mixture was centrifuged at 2500 rpm for 3 minutes, and the resulting clear liquid phase was separated. Absorbance of the clear phase was then measured using a UV/VIS spectrometer (Optima, SP-3000, Tokyo, Japan) at 540 nm wavelength. This entire procedure was conducted thrice (Gunathilake *et al*., 2018a). The level of hemolysis was calculated using Eq. 2 and the results are mentioned in table 1.

$$\% \text{ inhibition of hemolysis} = 100 \times \frac{1 - \text{Absorbance of sample}}{\text{Absorbance of Control}} \quad \text{….(Eq. 2)}$$

BSA-denaturation assay

The experiment followed a revised approach based on *Gunathilake et al.* 2018. In summary, a mixture comprising 1% bovine albumin (0.2mL), 20µg/mL CvB (0.02mL), and pH 6.4 PBS (phosphate buffered saline 4.780mL) was gently combined. Subsequently, the mixture was incubated in a water bath at 37ºC for 15 minutes and then heated to 70ºC for 5 minutes. Once cooled, the absorbance of the solutions was assessed at

660 nm using a UV/VIS spectrometer (Optima, SP-3000, Tokyo, Japan). A PBS (pH 7.4) devoid of the sample served as the control, and the % inhibition of protein denaturation was determined using Eq. 03 (Gunathilake *et al*., 2018b) and the results are mentioned in table 1.

$$\%\ \text{inhibition of denaturation} = 100 \times \frac{1\text{- Absorbance of sample}}{\text{Absorbance of Control}} \quad \text{(Eq. 3)}$$

Antiglycation assays

Congo-red binding assay

Detection of β-amyloid formation was executed by following the method described by *Miroliaei et al.* (2017). In brief, 100µL of Congo red solution and 400 µL of PBS (pH 7.4) were mixed with 100µL of 0.25mg/mL of CvB or a control (BSA + Glucose). The mixture was kept in the dark for 20 minutes at 25°C, following the measurement of absorbance at 530 nm wavelength using a UV/VIS spectrometer (Optima, SP-3000, Tokyo, Japan) (Miroliaei *et al*., 2017) and the outcomes are mentioned in table 2.

Fructosamine assay

The concentration of fructosamine (aminodeoxy sugar) in control and glycated albumin samples, was measured using the nitro-blue tetrazolium (NBT) assay as described by Tupe *et al.* (2017). A 0.75 mM NBT solution was prepared in a carbonate buffer (0.1 M, pH 10.35). The assay involved incubating 0.8 mL of the NBT solution with 40 µL of glycated samples for 30 minutes at 37 °C. Absorbance was measured at 530 nm using a UV/VIS spectrometer (Optima, SP-3000, Tokyo, Japan). The fructosamine concentration was then calculated using a standard 1-deoxy-1-morpholinofructose curve and expressed in µM/mg of protein (Y = 0.00X + 0.017, r = 0.981) (Tupe *et al*., 2017) results are displayed in table 2.

Free carbonyl group estimation

The carbonyl content in glycated samples was measured using the method described by *Ashraf et al.* (2015). A DNPH solution (10mM) was prepared in 2.5M HCl. Glycated sample (500µL) was incubated with 500 µL of the DNPH solution for 1 hour at room temperature with subsequent addition of 20% TCA (1.0mL) waited the sample to precipitate. The precipitate was washed with a ethyl acetate and ethanol mixture in 1:1 (v/v) ratio, followed by addition of in 1mL of 6 M urea. The absorbance was measured at 365 nm using a UV/VIS spectrometer (Optima, SP-3000, Tokyo, Japan). The concentration of protein carbonyl groups was determined using a molar extinction coefficient (ε) of 21 mM^{-1} cm^{-1} at 365 nm and expressed in nM per mg of protein (Ashraf *et al*., 2015) and results are displayed in table 2.

Preparation of Wistar albino rats

Wistar albino rats of either sex having (120±20 g in body weight) in total no 48 were placed in the animal house of the Faculty of Pharmacy, Bahauddin Zakariya University Multan, Pakistan. All rats were housed in polycarbonate cages of 7 x 34 x 18 cm^3, in 8 cages with a maximum of six rats per cage, 12–12 hours of light and dark, respectively and at typical temperature and humidity levels of 25±2°C. Animals were given a conventional animal food and unlimited access to water. The experimental protocol was approved by the Institutional Animal Ethics Committee at the Faculty of Pharmacy and Pharmaceutical Sciences, University of Karachi. The experiment was conducted in compliance with the committee's regulations for the supervision and management of animal experiments, as per Institutional Bioethical Committee Approval No. IBC KU-289/2022.

In-vivo methodology

Animal study was performed according to standard protocol with slight modifications. *Wistar albino* rats (n=48) weighing (120±20 g) was habituated for 14 days prior to start of experiment then all the groups are continued with listed treatments.

Group I: It was called as normal control (NC) and consists of 6 animals, receives normal saline at the rate of 5mL/kg of body weight per-oral for complete period of study (84days).

Group II: It was called as obesity induction group and consists of 42 rats, receives 3 ml/kg body weight of High Fat High Sugar Diet (HFHSD) that composed of Vanaspati ghee and coconut oil (3:1) and 10 mL/kg 25% dextrose water P.O. for 56 days. After 56 days these 42 animals were divided into following different three groups B1 (n=6), B2 (n=6) and B3 (n=30).

Group B1: It was called as obesity control (OC) group and consists of six animals. All animals were fed with 3 ml/kg of body weight HFHSD for remaining (28 days) four weeks of study.

Group B2: It was called as obesity treatment (OT) group, rats were continued to fed with high fat high sugar diet (HFHSD) along with atorvastatin (standard drug) 60 mg/kg orally for further 28 days.

Group B3: Obesity-diabetes group, rats (n=30) were nourished with high fat high sugar diet (HFHSD) along with streptozotocin (65 mg/kg) interperitoneally prepared in pH 4.5 citrate buffer. Blood glucose level was checked after 48 hours after injection. Animals showing blood glucose level ≥200 mg/mL were arbitrarily split up into following 5 groups C-G (n=6) and were fed with HFHSD for complete period of study (84 days).

Group C: It was called as obesity-diabetes control (ODC) group, consists of 6 animals and was administered normal saline orally 5 mL/kg of body weight for 28 days.

Group D: It consists of six animals and called as obesity-diabetes treatment (ODT) group, rats in this group were administered with Glibenclamide (10 mg/kg) and atorvastatin (60 mg/kg) for 28 days.

Group E: It was called as obesity-diabetes treatment (ODCvB1) group containing 6 animals in which rats were feeded with CvB (100 mg/kg) orally for 28 days.

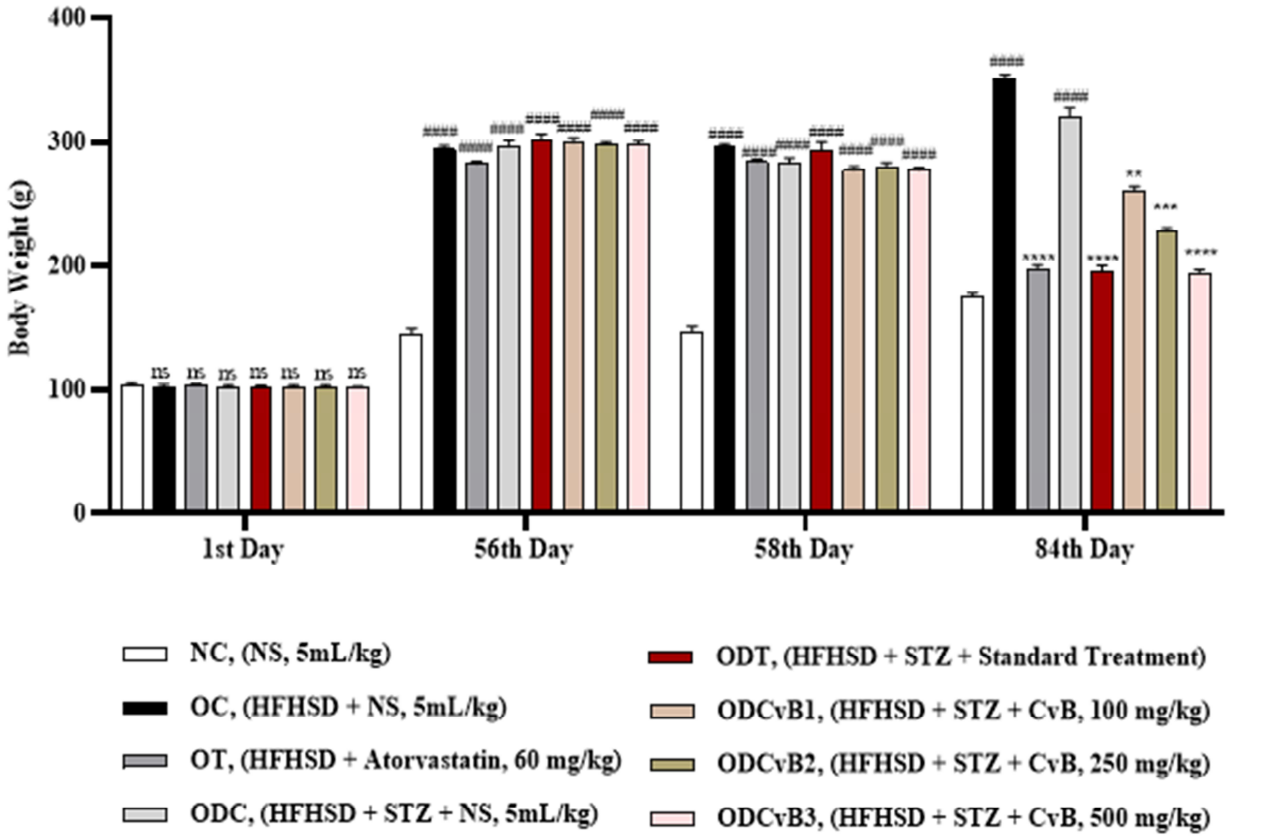
Table 1: Anti-inflammatory potential of *Cinnamomum verum* bark extract (CvB)

S. No.	Parameter	Plant extract	Standard
1	Proteinase inhibition activity	76 ± 1.06 %	84 ± 1.05 %
2	Heat induced hemolysis	59±1.02 %	86 ± 1.05 %
3	*BSA denaturation assay	48.2 ± 1.04 %	54.2 ± 1.05 %

*Where BSA: Bovine serum albumin

Table 2: Antiglycation potential of *Cinnamomum verum* bark extract (CvB)

S. No.	Parameter	Plant extract	Standard
1	Congo red assay	0.022 absorbance	0.12 absorbance
2	Fructosamine assay	33.3±0.04 %	
3	Free carbonyl group estimation	20.3±0.02 %	



Each group (n = 6) has its mean ± standard error of mean (SEM) was examined using two-way ANOVA using Tukey's post hoc test. At 1st day all the groups showed non-significant (ns) variations while comparing to normal control (NC) group. After 56 days' period, all the groups exhibited p<0.001: very significant (###) while comparing to normal control (NC) group. After 58 days' period, all the groups exhibited p<0.001: very significant denoted by (###) while comparing to normal control (NC) group. After 84 days' period, when the obesity control (OC) group was compared with obesity treatment (OT) group and obesity diabetes control (ODC) group is compared to treatment groups (ODT, ODCvB1, ODCvB2 and ODCvB3), results exhibiting p<0.0001: highly significant denoted by (****) p<0.001: very significant denoted by (***), p<0.01 more significant denoted by (**), p<0.05: significant denoted by (*) and p>0.05 are considered non-significant denoted by (ns). The NC group while compared with OC group and ODC group, p<0.001: very significant results are denoted with (###).

Fig. 1: Changes in body weight of *Wistar albino* rats.

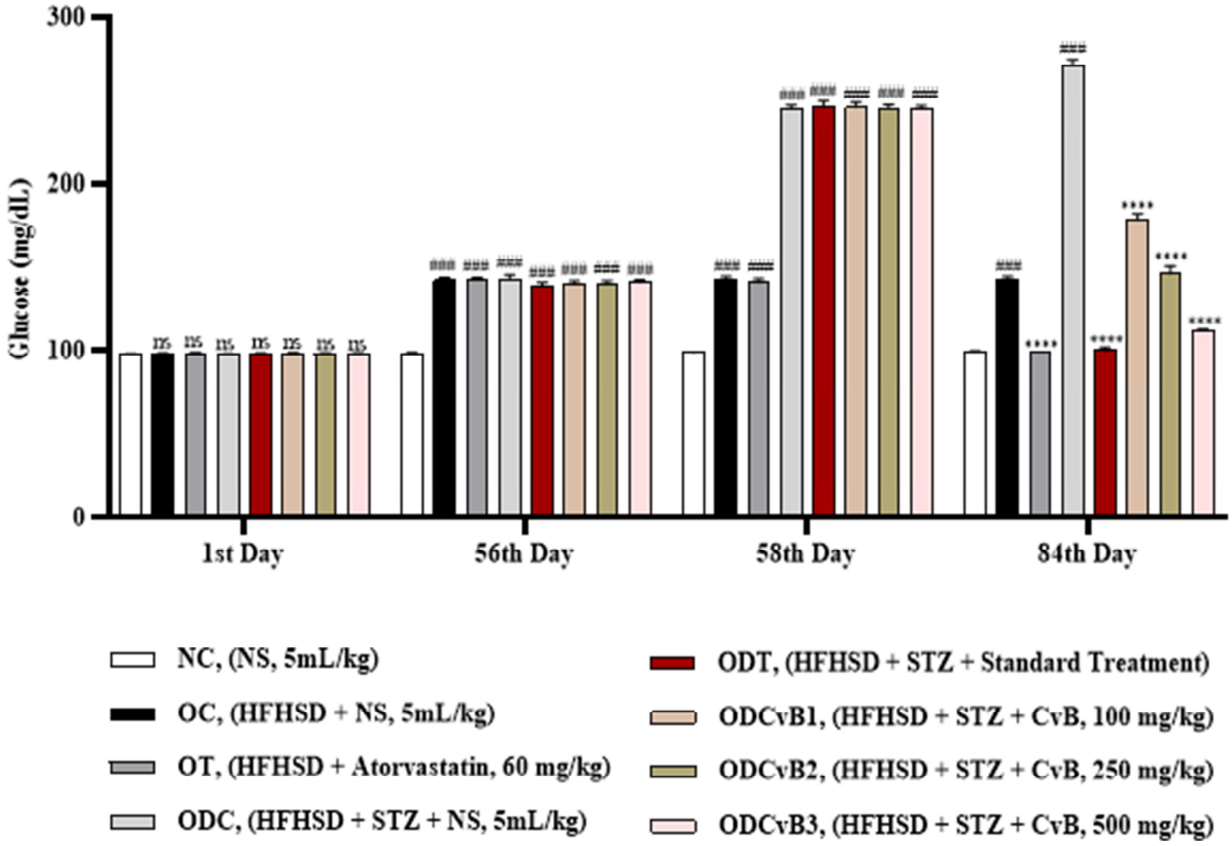


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Fig. 2: Changes in blood glucose concentration of *Wistar albino* rats.

Group F: Obesity-Diabetes Treatment (ODCvB2) group, in this group 6 rat were provided with CvB (250 mg/kg) for a period of remaining period (28 days).

Group G: Obesity-Diabetes Treatment (ODCvB3) group in which rats (6) were given with CvB (500 mg/kg) for 28 days (Munshi *et al*., 2014, Gomez-Dominguez *et al*., 2006). Body weight and blood sugar level was measured at 1st day, 56th day, 58th day and 84th day.

Blood samples for lipid profile (low-density lipoproteins, total cholesterol high density lipoproteins and triglycerides) and liver function test (Aspartate transaminase, total bilirubin, alkaline phosphatase and alanine transaminase) were collected by closed cardiac puncture at start, after 56 days of HFHSD and after 84 days' study period and preserved at -20℃. The body weight of all animals was also measured at 1st day, at 56th day of HFHSD, at 58th day and at 84th day of complete study period.

STATISTICAL ANALYSIS

Every result was revealed as the mean of the standard error of n=6 for every set, Graph Pad Prism 9.0.1 (La Jolla, CA, USA) was used for statistical evaluation for determining the results by two-way ANOVA and Tukey's test, which was used to determine the significance between different groups by setting P≤0.05.

Fourier transform infrared (FT-IR) spectroscopy

The test sample 0.5g of CvB was evaluated for the presence of functional groups by using this technique. The sample was put on the ATR-FTIR spectrophotometer (Bruker IR affinity 1 model Japan Limited) with a wavelength of 400-4000 cm^{-1} equipped with Bruker

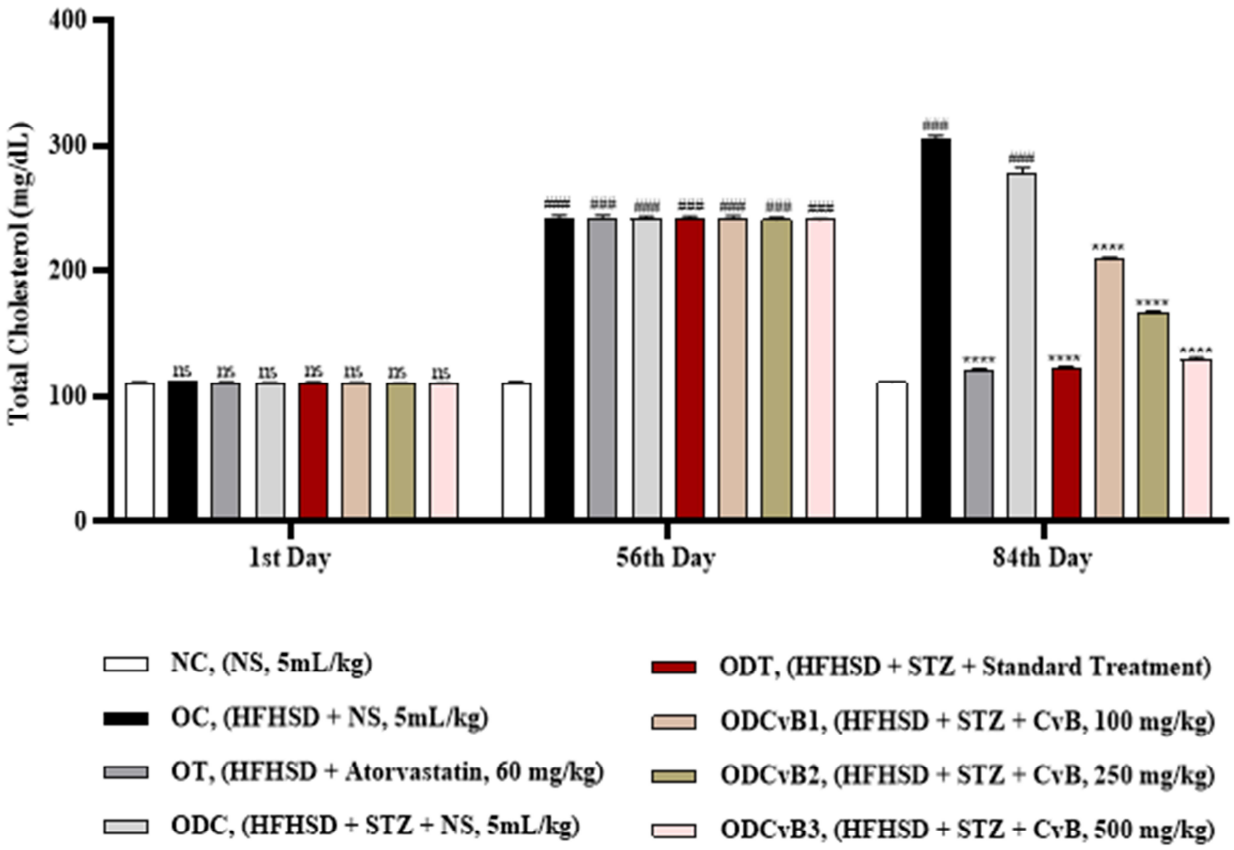

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Fig. 3: Changes in Total cholesterol levels of *Wistar albino* rats.

OPUS software. Different wavelengths of Infrared light were absorbed by the sample. The energy that was absorbed was transferred to vibrational energy, which produced the signals that are examined by the detector. The computer was used to evaluate compounds with various functional groups and resultant peaks were examined (Jain *et al*., 2016). The results are explained in fig. 10.

High-performance liquid chromatography (HPLC) assay

The plant material (5mg/mL) was added in solvent (methanol) and allowed to pass through syringe filter (0.45 micron, Millex ®). HPLC analysis was conducted on a Spectra-Physics SP 8800/8810LC pump in conjugation with a Varian 9065 polychrom diode-array detection system. The mobile phase that consists of acetonitrile and distilled water (ACN: H_2O; 60:40) and elution were identical to the analytical run. The flow rate was 1 ml/min and 500 µL of CvB solution (5 mg/mL) was injected on a Supelco® HPLC column (12 ×260 mm, 5 µm) (Sigma Aldrich), with a 17 min linear gradient at 25℃ (de Paz *et al*., 2010). The following phenolic compounds were used as standards for the detection of flavonoids in the CvB sample: chlorogenic acid, ferulic acid, rutin, coumarin, and thymoquinone, and the peaks of the sample were compared with standards. The findings of the HPLC analysis are mentioned in fig. 11.

Ethical approval

The Institutional Animal Ethics Committee, Faculty of Pharmacy and Pharmaceutical Sciences, University of Karachi, approved the experiment's protocol and the experiment was conducted in compliance with the Panel's rules for the monitoring and administration of animal experiments under Institutional Bioethical Committee Approval No. IBC KU-289/2022.

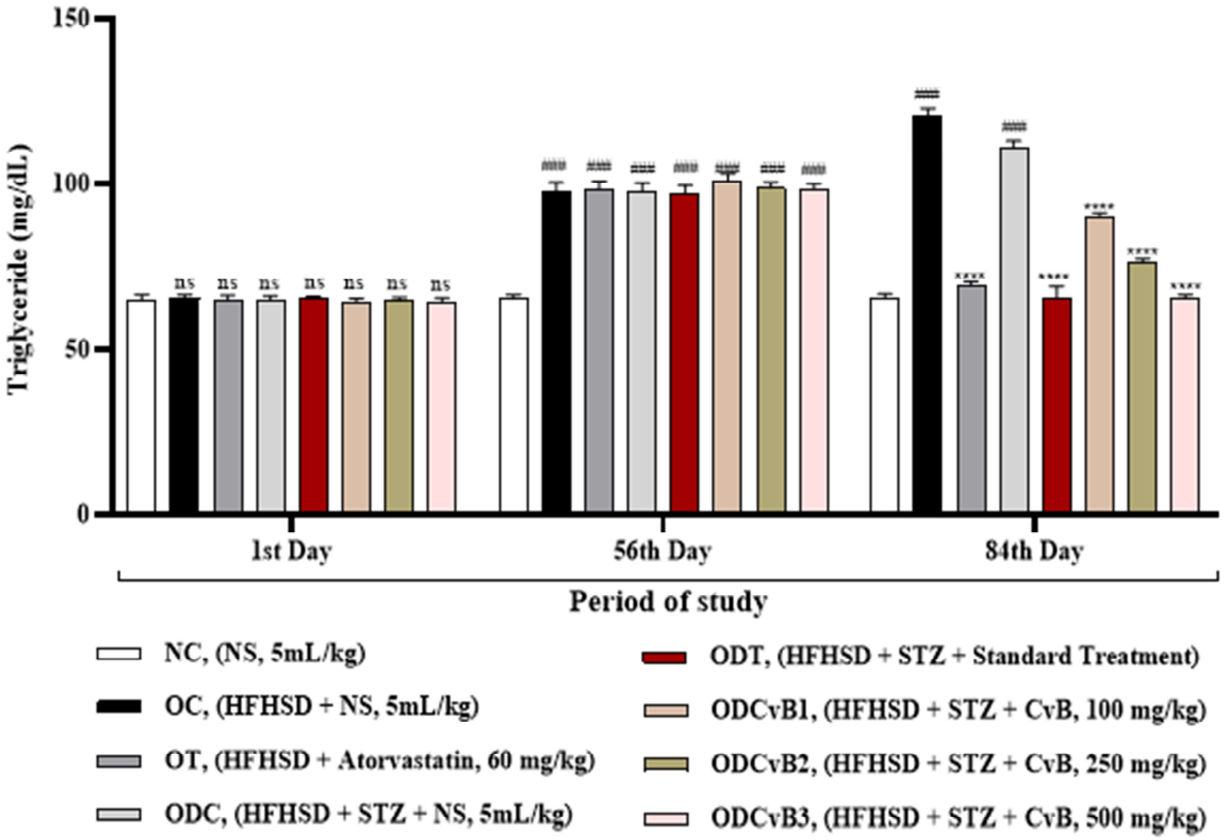

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Fig. 4: Changes in triglycerides levels of *Wistar albino* rats.

RESULTS

Anti-inflammatory potential of CvB by different methods (proteinase inhibition activity, heat induced hemolysis, BSA denaturation) are shown in table 1. Similarly results of Antiglycation activity by different methods like condo red assay, fructosamine assay and free carbonyl group estimation are presented in table 2. The influence of CvB on the body weight of rats over various days is illustrated in fig. 1. Effects of CvB on blood glucose level are shown in fig. 2. The impact of CvB on the lipid profile, including total cholesterol, triglycerides, high-density lipoproteins, and low-density lipoproteins, is depicted in fig. 3-6. Likewise, the effect of CvB on liver parameters such as aspartate amino transferase, alanine amino transferase, and alkaline phosphatase is illustrated in fig. 7-9. FT-IR spectra showing different functional groups are presented in fig. 10 and HPLC fingerprint of CvB extract and different standards drugs is shown in fig. 11.

DISCUSSION

Plants are always been an inspirational source for many researchers because 80% people from all over the world depends upon plant-based medicines. Large numbers of plants are constantly being screened for their possible pharmacological value particularly for their anti-inflammatory, hypoglycemic, anti-fertility, bronchodilator, antioxidant and hepatoprotective properties (Mallhi *et al*., 2014). Clinical research is needed to evaluate the pharmacological and toxicological profiles of these herbal drugs, develop animal models for toxicity and safety assessment, and identify active components to develop effective medications (Modak *et al*., 2007). *In vivo* benefits of *Cinnamomum verum* include attenuated diabetes-associated weight loss, reduced fasting blood glucose, lowered LDL and HbA1c, increased HDL cholesterol and circulating insulin and improved metabolic derangements linked to insulin resistance (Ariyanto *et al*., 2021). In current research the

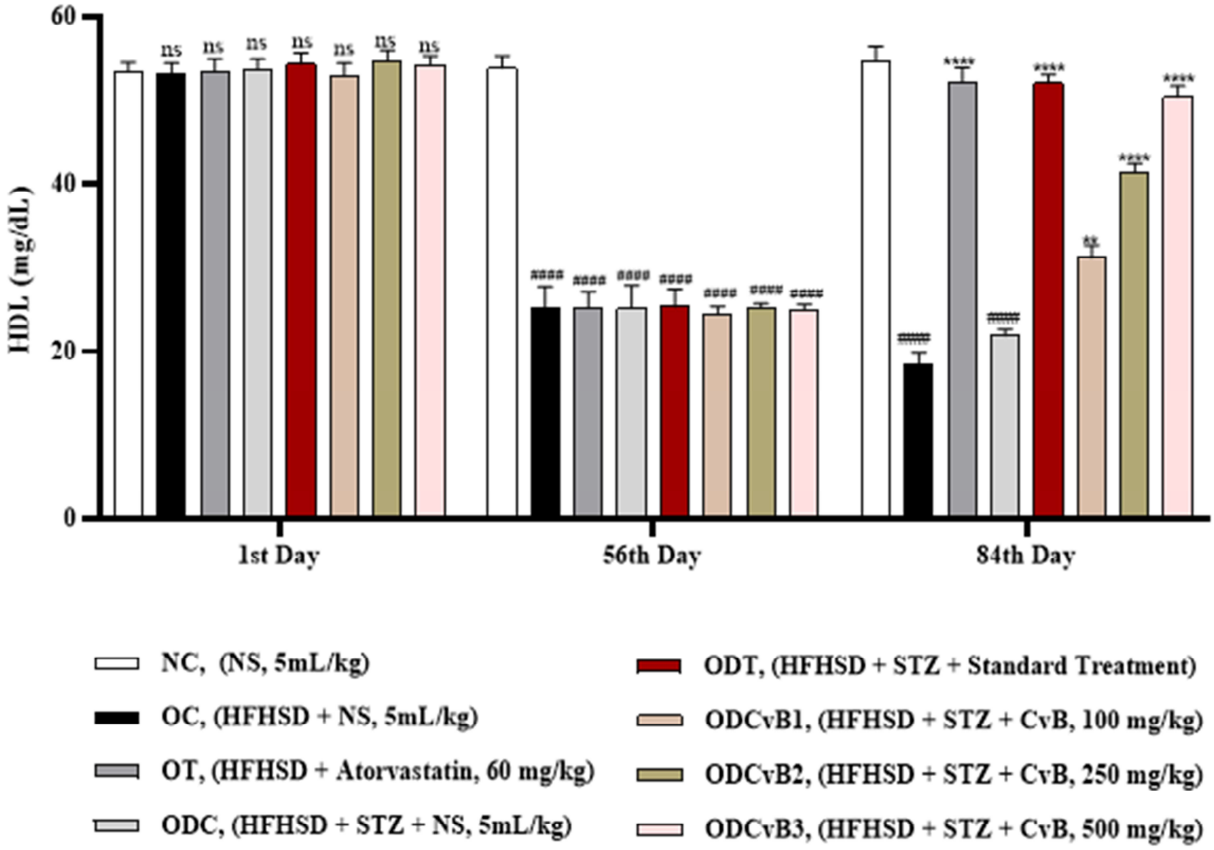

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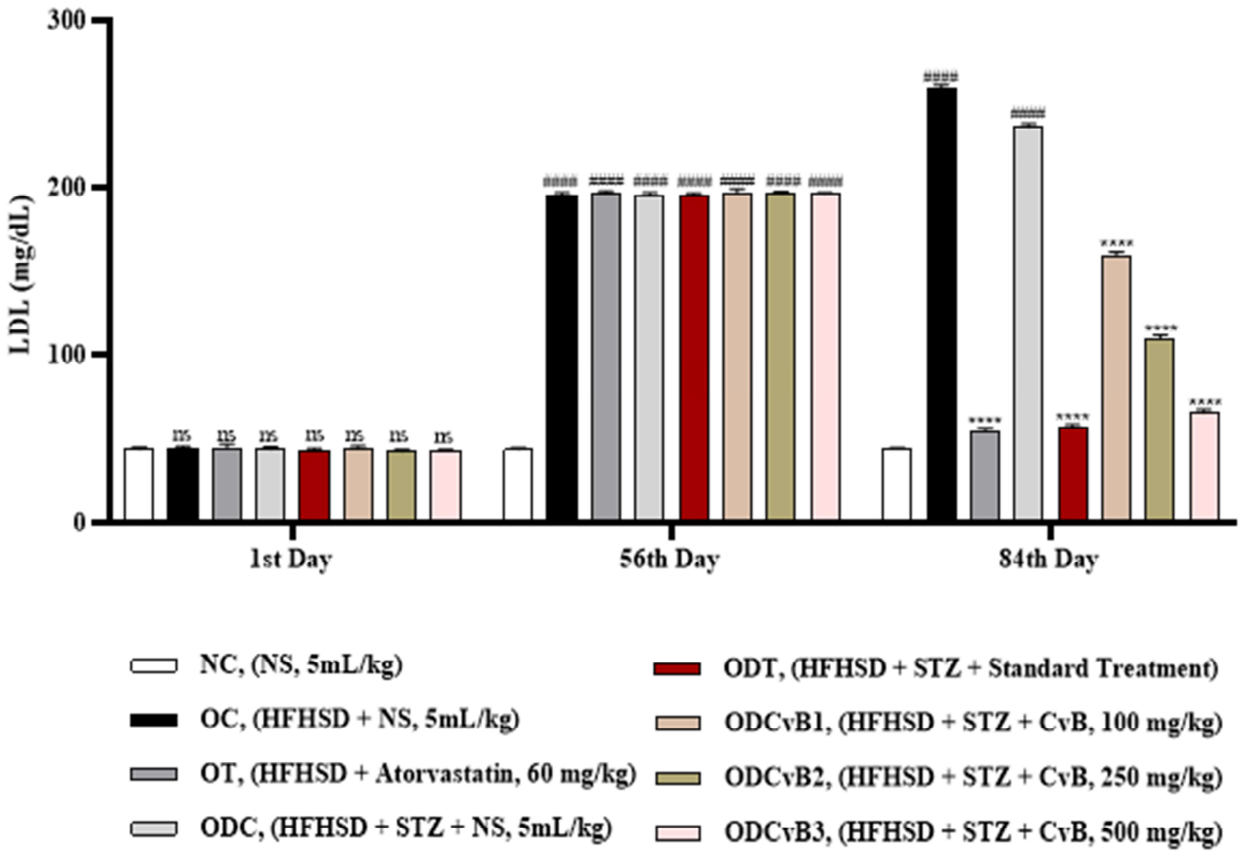
Fig. 5: Changes in High density lipoproteins (HDL) levels of *Wistar albino* rats.

anti-inflammatory, anti-obesity and anti-diabetic efficacy of *Cinnamomum verum* J. Presi bark extract was assessed using *in vitro* and *in vivo* diagnostic markers.

Diabetes mellitus is characterized by an insulin deficit, decreased protein levels of insulin receptors, chronic inflammatory state and persistent oxidative stress. The phytochemical showed potent antioxidant actions and anti-inflammatory effects by reducing levels of NF-kB, TNF-α and IL-6 thus possesses antihyperglycemic and anti-dyslipidemic effect (Scarpa *et al*., 2024). In our investigation, CvB demonstrated 48.2±1.04% inhibition which is notable protective effect against the denaturation of BSA. This inhibition may be due to the presence of flavonoids, alkaloids and polyphenolic compounds in the extracts (Kariawasam *et al*., 2017). Multiple reports substantiate that tissue damage in the body is primarily facilitated by proteinases during inflammatory processes. Therefore, inhibiting proteinases is a beneficial approach in the management of inflammatory responses (Mohanty *et al*., 2024). In our study, we observed proteinase inhibition was 76±1.06%, suggesting a relatively significant contribution to anti-inflammatory mechanism of CvB (Chopade *et al*., 2012). Additionally, the modulation of inflammation is elucidated by the release of lysosomal contents resulting from cellular breakage.

Considering the close resemblance of the cell membrane of red blood cells (RBCs) to lysosomes, agents that prevent hemolysis of red blood cells can offer valuable insights into their anti-inflammatory mechanisms (Anyasor *et al*., 2017, Pagliari *et al*., 2023). CvB showed significant stabilization effect (59±1.02 %) against heat induced hemolysis of RBC membrane. This suggested that CvB may contain the anti-inflammatory compounds like alkaloids, polyphenols and triterpenoids. The process of production of irreversible heterogeneous byproducts known as advance glycated end products (AGEs) as a

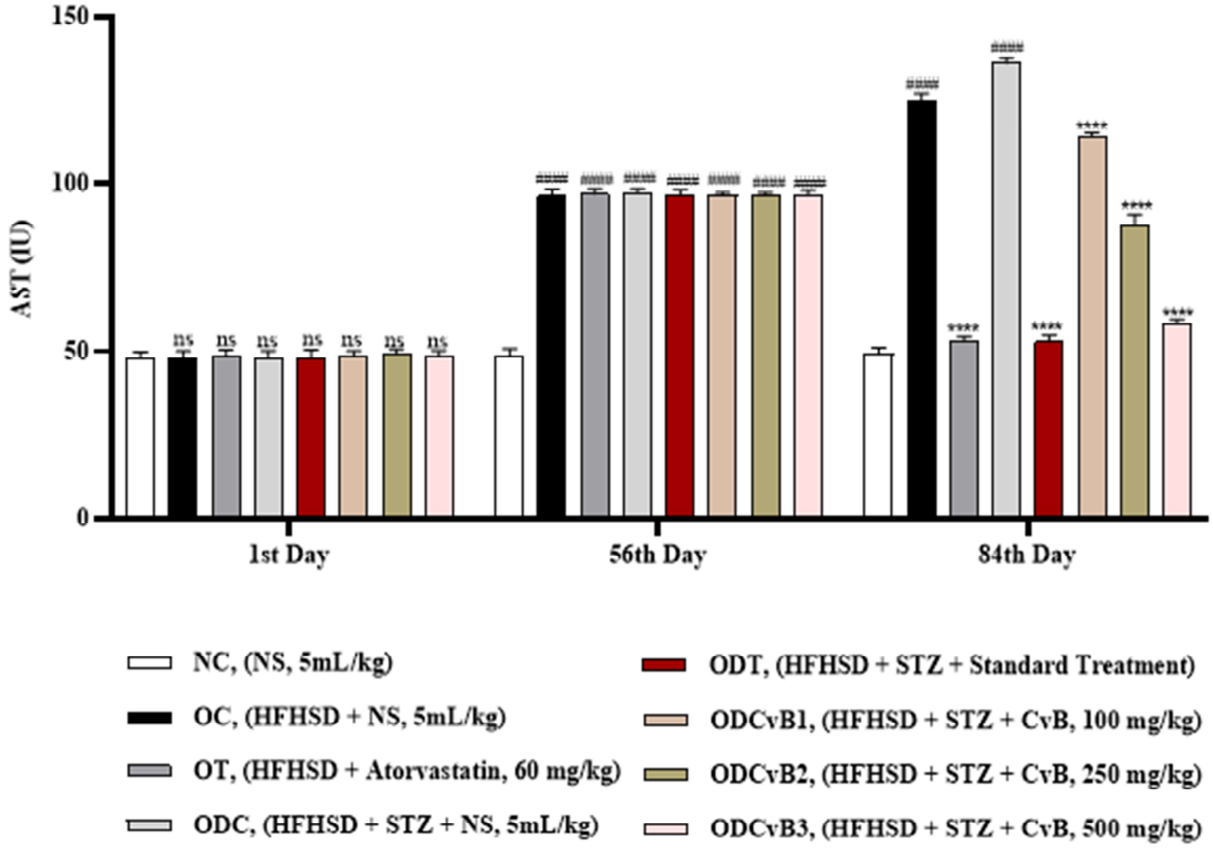


Each group (n = 6) has its mean ± standard error of mean (SEM) is examined using two-way ANOVA using Tukey's post hoc test. At 1st day all the groups showed non-significant (ns) variations while comparing to normal control (NC) group. After 56 days' period, all the groups exhibited p<0.001: very significant (###) while comparing to normal control (NC) group. After 58 days' period, all the groups exhibited p<0.001: very significant denoted by (###) while comparing to normal control (NC) group. After 84 days' period, when the obesity control (OC) group was compared with obesity treatment (OT) group and obesity diabetes control (ODC) group is compared to treatment groups (ODT, ODCvB1, ODCvB2 and ODCvB3), results exhibiting p<0.0001: highly significant denoted by (****) p<0.001: very significant denoted by (***), p<0.01 more significant denoted by (**), p<0.05: significant denoted by (*) and p>0.05 are considered non-significant denoted by (ns). The NC group while compared with OC group and ODC group, p<0.001: very significant results are denoted with (###).

Fig. 6: Changes in Low density lipoproteins (LDL) levels of *Wistar albino* rats.

result of chemical alteration in variety of proteins is called glycation. The accumulation of AGEs plays a central role in the aging process and the pathogenesis of diabetes and obesity (Jariyapamornkoon *et al*., 2013). Both microvascular and macrovascular complications of diabetes progress with the accumulation of AGEs. Various types of AGEs contribute significantly to the advancement of diabetic pathologies, including β-amyloid formation, fructosamine adduct formation and free carbonyl formation. These processes are implicated in the multifaceted mechanisms underlying the complications associated with diabetes (Alrouji *et al*., 2023). In our analysis of CvB, we observed equal absorbance levels compared to the control (BSA + glucose), indicating a potential protective role against advanced glycation end products (AGEs) formation. However, in the Fructosamine assay and free carbonyl estimation assay, inhibition levels of 33.3±0.04% and 20.3±0.02% were recorded respectively. Consequently, we concluded that CvB may exhibit moderate levels of inhibition against AGEs formation.

In our research, we developed an obesity-diabetes model in rats by feeding them a high-fat high-sugar diet for 8 weeks and administering a single dose of streptozotocin (STZ), with minor adjustments. This model showed noticeably higher fasting blood glucose levels compared to the rats in the normal control group (Gomez-Dominguez *et al*., 2006, Sreejesh *et al*., 2017). Throughout the study, we carefully weigh body weights, noting a substantial increase in the obesity-diabetes model (ODC) group. This indicates successful obesity development in the model, marked by increased adipose tissue mass and accompanying metabolic abnormalities like elevated levels of glucose, leptin, or insulin. These findings emphasize the relevance and credibility of our established model in simulating the intricate relationship between obesity and diabetes (Collins *et al*., 2018).

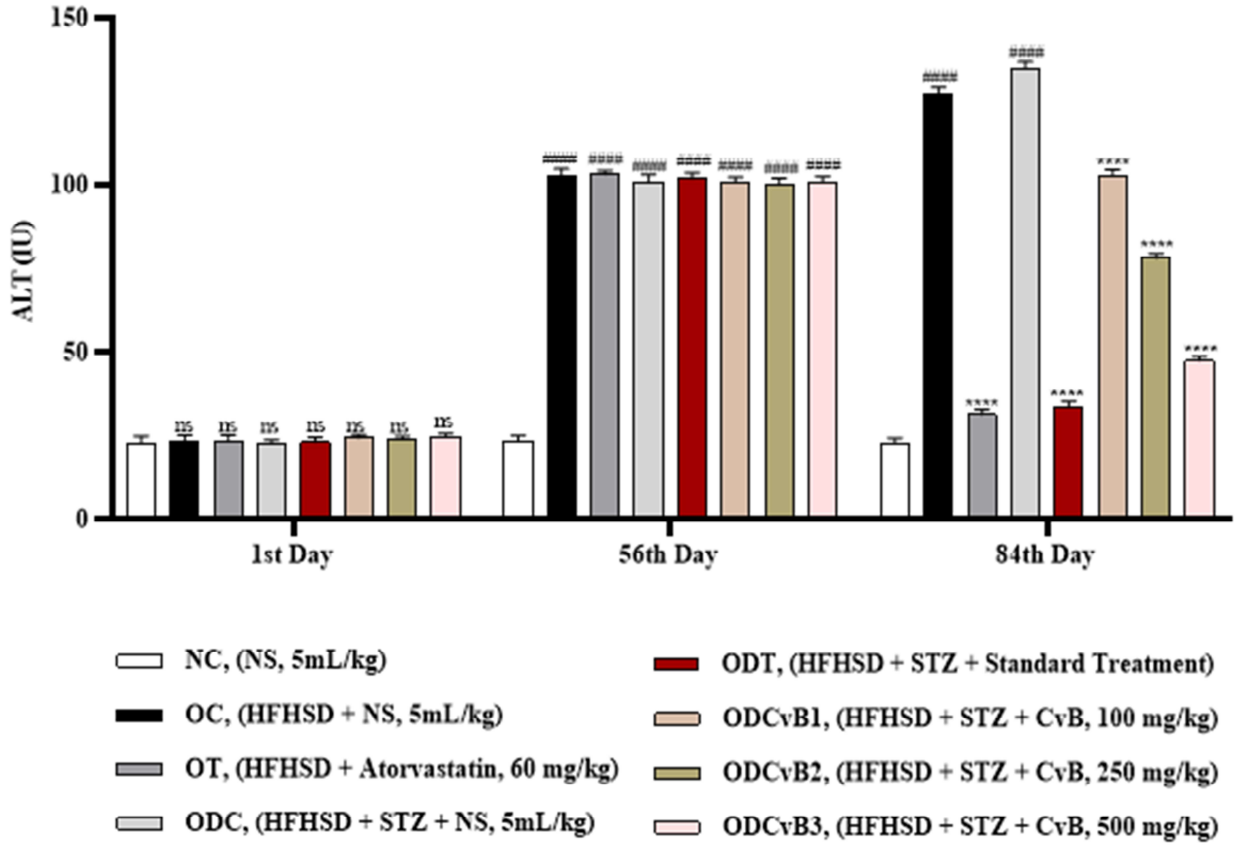


Each group (n = 6) has its mean ± standard error of mean (SEM) is examined using two-way ANOVA using Tukey's post hoc test. At 1st day all the groups showed non-significant (ns) variations while comparing to normal control (NC) group. After 56 days' period, all the groups exhibited p<0.001: very significant (###) while comparing to normal control (NC) group. After 58 days' period, all the groups exhibited p<0.001: very significant denoted by (###) while comparing to normal control (NC) group. After 84 days' period, when the obesity control (OC) group was compared with obesity treatment (OT) group and obesity diabetes control (ODC) group is compared to treatment groups (ODT, ODCvB1, ODCvB2 and ODCvB3), results exhibiting p<0.0001: highly significant denoted by (****) p<0.001: very significant denoted by (***), p<0.01 more significant denoted by (**), p<0.05: significant denoted by (*) and p>0.05 are considered non-significant denoted by (ns). The NC group while compared with OC group and ODC group, p<0.001: very significant results are denoted with (###).

Fig. 7: Changes in aspartate aminotransferase (AST) levels of *Wistar albino* rats.

Interestingly, our observations showed that while the obesity-diabetes model (ODC) group experienced a significant increase in body weight, the actual weight gain in grams was lower compared to the obesity control (OC) group, which received a High-Fat High-Sugar Diet (HFHSD) alone for a similar duration. This finding suggests that inducing obesity and diabetes together in the ODC group might influence the nature or distribution of weight gain, indicating nuanced metabolic responses within this integrated model (Yang *et al*., 2016). *Wistar albino* rats within the obesity control (OC) and obesity diabetes control (ODC) groups exhibited a notable and statistically significant increase (p<0.005) in body weights. However, following the administration of CvB (100, 250 and 500mg/kg), a noteworthy (p<0.001) decline in body weight was observed in the treatment groups OT, ODT, ODCvB1, ODCvB2 and ODCvB3. The fluctuation in body weight observed during the study period may be attributed to the influence of streptozotocin (STZ), a phenomenon documented in previous studies to limit weight gain (Zhu *et al*., 2018). The administration of CvB resulted in a reduction in the increase of body weight, with this decrease being more pronounced in the ODCvB3 group as compared to the lower doses of CvB. At 84th day of study *Wistar albino* rats (n=18) of obesity diabetes treatment groups (ODCvB1, ODCvB2 and ODCvB3) treated with different doses of CvB 100, 250 and 500mg/Kg bwt show cased a concentration dependent decline in body weight of *Wistar albino* rats 260.8±3.62 g, 227.6±2.86 g and 194.8±2.62g respectively. ODCvB3 group exhibited p<0.001: very significant decline in body weight while comparing with obesity diabetes control group (ODC) having 320.2±8.06g as shown in fig. 1.

Blood glucose level showed a noticeable elevation (p< 0.001) in ODC groups. After CvB administration at the increasing doses of (100, 250 and 500 mg/Kg of body weight) noticeable (p<0.001) lessening in blood glucose

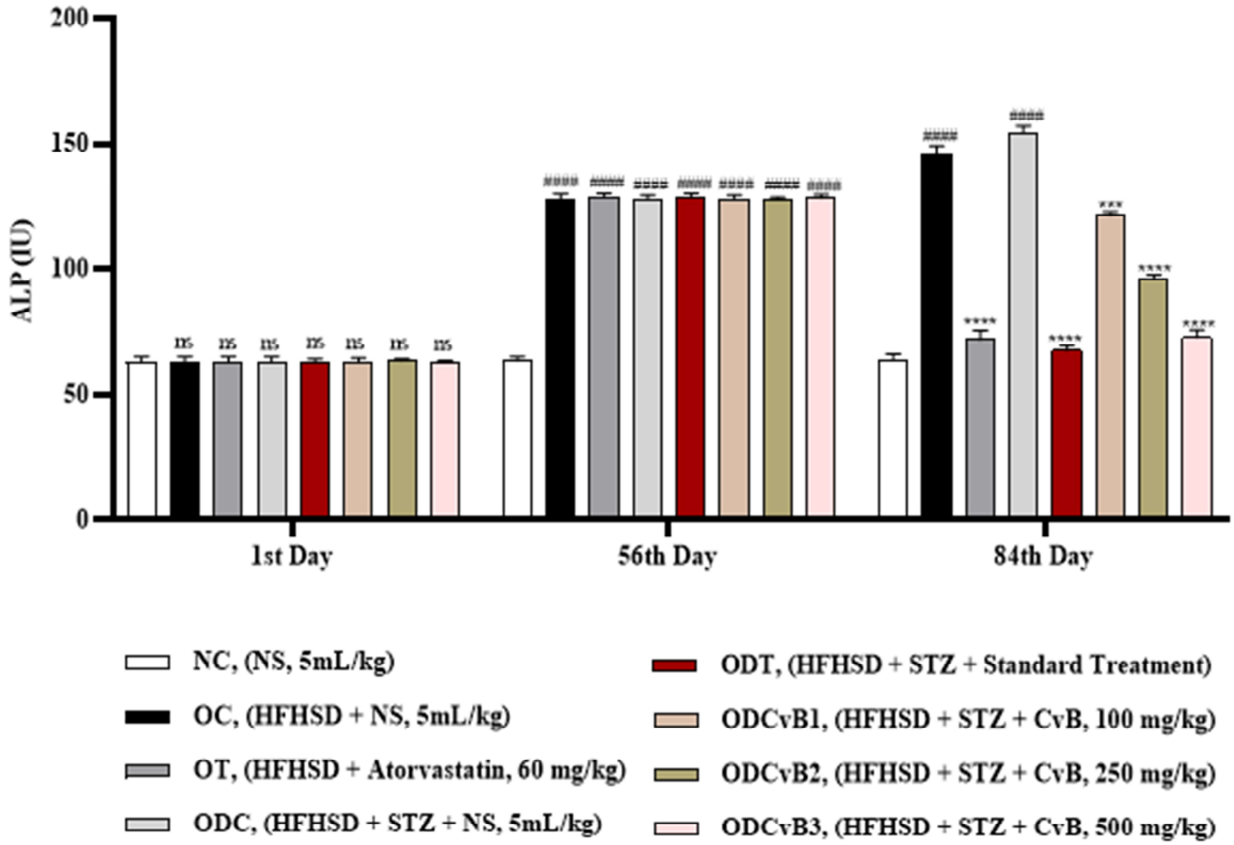


Each group (n = 6) has its mean ± standard error of mean (SEM) is examined using two-way ANOVA using Tukey's post hoc test. At 1st day all the groups showed non-significant (ns) variations while comparing to normal control (NC) group. After 56 days' period, all the groups exhibited p<0.001: very significant (###) while comparing to normal control (NC) group. After 58 days' period, all the groups exhibited p<0.001: very significant denoted by (###) while comparing to normal control (NC) group. After 84 days' period, when the obesity control (OC) group was compared with obesity treatment (OT) group and obesity diabetes control (ODC) group is compared to treatment groups (ODT, ODCvB1, ODCvB2 and ODCvB3), results exhibiting p<0.0001: highly significant denoted by (****) p<0.001: very significant denoted by (***), p<0.01 more significant denoted by (**), p<0.05: significant denoted by (*) and p>0.05 are considered non-significant denoted by (ns). The NC group while compared with OC group and ODC group, p<0.001: very significant results are denoted with (###).

Fig. 8: Changes in alanine aminotransferase (ALT) levels of *Wistar albino* rats.

levels depending upon the concentration of CvB in ODCvB1, ODCvB2 and ODCvB3 groups when compared with ODC group. CvB significantly reduced blood glucose levels at higher doses of 500mg/Kg shown in fig. 2. Serum total cholesterol (TC) level displayed a substantial uplift (p<0.001) in obesity control (OC) and obesity diabetes control (ODC) groups. After treatment with CvB (100, 250 and 500mg/Kg), a momentous (p< 0.001) reduction in total cholesterol in ODCvB1, ODCvB2 and ODCvB3 group was noted depending upon the dose in comparison to ODC group in fig. 3. Substantial increase (p<0.001) in triglycerides (TG) level was observed in OC and ODC groups.

After treatment with CvB (100, 250 and 500mg/Kg) there was momentous (p<0.001) lessening of TG level in ODCvB1, ODCvB2 and ODCvB3 when compared with ODC group in fig. 4. Serum high density lipoproteins (HDL) showed decrease (p<0.001) in OC and ODC groups. After treatment with CvB (100, 250 and 500mg/Kg bwt) a significant (p<0.001) concentration dependent elevation in HDL level was noticed in ODCvB1, ODCvB2 and ODCvB3 when compared with ODC group as in fig. 5. There was increase (p<0.001) in serum low density lipoproteins (LDL) level in OC and ODC groups. After treatment of ODCvB1, ODCvB2 and ODCvB3 groups with CvB (100, 250 and 500mg/Kg) separately, there was a remarkable decline (p<0.001) in LDL level was observed depending upon the dose in comparison to ODC group shown in fig. 6. Level of serum AST (Aspartate Aminotransferase) increased (p<0.001) significantly in OC and ODC groups. After treatment with CvB (100, 250 and 500mg/Kg), a remarkable (p<0.001) reduction takes place depending on dose in AST level in different groups such as ODCvB1, ODCvB2 and ODCvB3 when compared with ODC group as shown in fig. 7.



Each group (n=6) has its mean ± standard error of mean (SEM) is examined using two-way ANOVA using Tukey's post hoc test. At 1st day all the groups showed non-significant (ns) variations while comparing to normal control (NC) group. After 56 days' period, all the groups exhibited p<0.001: very significant (###) while comparing to normal control (NC) group. After 58 days' period, all the groups exhibited p<0.001: Very significant denoted by (###) while comparing to normal control (NC) group. After 84 days' period, when the obesity control (OC) group was compared with obesity treatment (OT) group and obesity diabetes control (ODC) group is compared to treatment groups (ODT, ODCvB1, ODCvB2 and ODCvB3), results exhibiting p<0.0001: highly significant denoted by (****) p<0.001: very significant denoted by (***), p<0.01 more significant denoted by (**), p<0.05: Significant denoted by (*) and p>0.05 are considered non-significant denoted by (ns). The NC group while compared with OC group and ODC group, p<0.001: Very significant results are denoted with (###).

Fig. 9: Changes in alkaline phosphatase (ALP) levels of *Wistar albino* rats.

Serum Alkaline phosphatase (ALP) level showed a noteworthy increase (p<0.005) in OC and ODC groups. After treatment with CvB (100, 250 and 500mg/kg) a considerable decline (p<0.005) in ALP level was noticed in ODCvB1, ODCvB2 and ODCvB3 depending upon the dose when compared with ODC group as shown in fig. 8. Serum Alanine aminotransferase (ALT) level was elevated (p<0.005) in OC and ODC groups. After treatment with different doses of CvB, there was considerable (p<0.005) decline in ALT in dose dependent manner in ODCvB1, ODCvB2 and ODCvB3 when compared with ODC group fig. 9.

IR spectra of dry CvB were recorded by FTIR is presented in fig. 10. On FTIR the difference. between the spectra considered as proof of the transformation. The band observed in 3378 cm^{-1} as alcohol (O-H stretching) or as aliphatic primary amines (N-H stretching), 2922 and 2858cm^{-1} as alkanes (C-H Stretching), 1676cm^{-1} as alkene (C=C), 1723cm^{-1} as aldehyde (-C=O Stretching), 1615 and 1670cm^{-1} as carbonyl (C=O), 1518cm^{-1} as alkane methyl group (C-H stretching), 1450cm^{-1} as phenol or alcohol (Ph-OH/ O-H Bending), 1123cm^{-1} as tertiary alcohol (C-O), 1041 cm^{-1} as sulfoxide (S=O group), 1253 cm^{-1} as amine (C-N Stretching), 978 s/cm as carbonyl (O-H Bending) and 876 s/cm as trisubstituted or disubstituted alkanes (C-H bending) are labeled in the extracted spectrum. The bands observed in FT-IR graph showed the presence of aliphatic primary amines, alcohols, phenols, alkanes, alkenes, aldehydes, carbonyl compounds, methyl groups, phenols, tertiary alcohols, amines and sulfoxides. HPLC chromatogram depicts the presence of thymoquine and coumarin α-cystein. Thymoquinone (TQ) possesses anti-inflammatory and antioxidant effects by scavenging free radicals and enhancing the activity of internal antioxidant enzymes (Alzahrani *et al*., 2024). Therefore thymoquinone used as antiviral, anticancer, antibacterial, immunomodulatory, anticoagulant, antipsychotic,

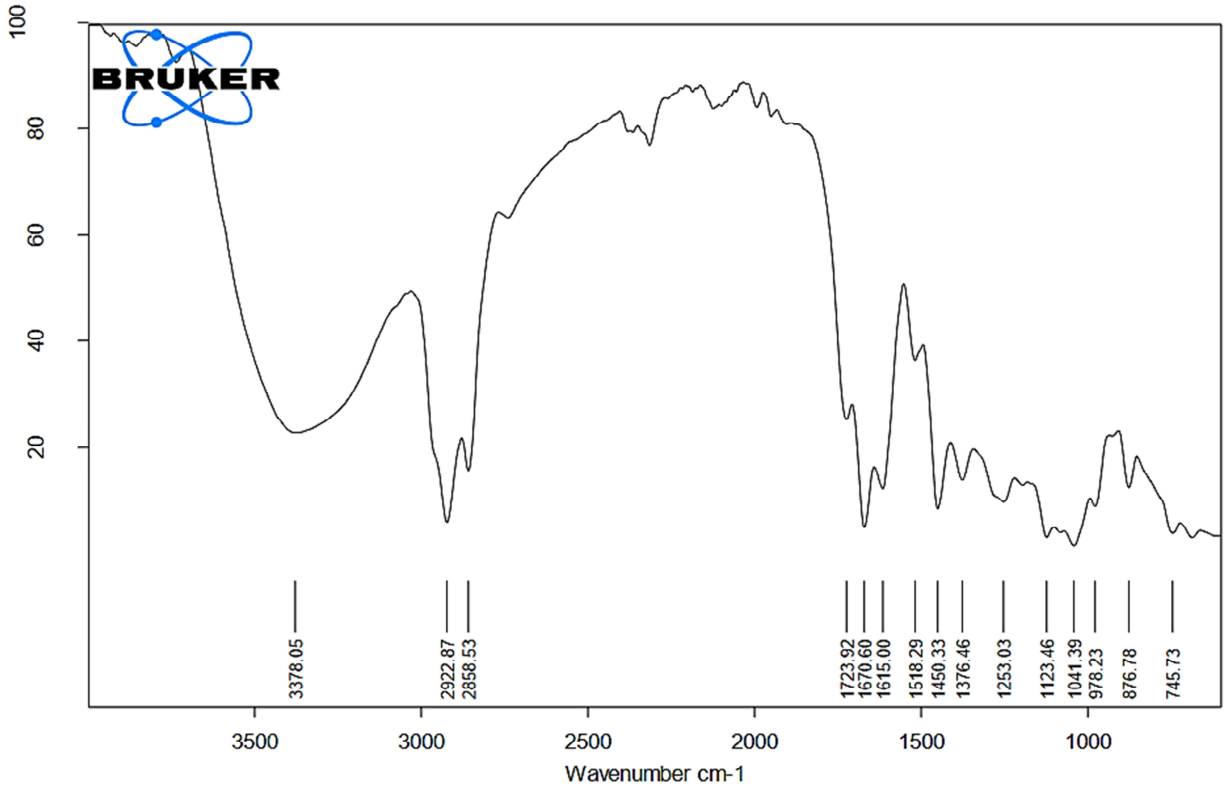


Fig. 10: FT-IR Spectrum of *Cinnamomum verum* bark extract (CvB).

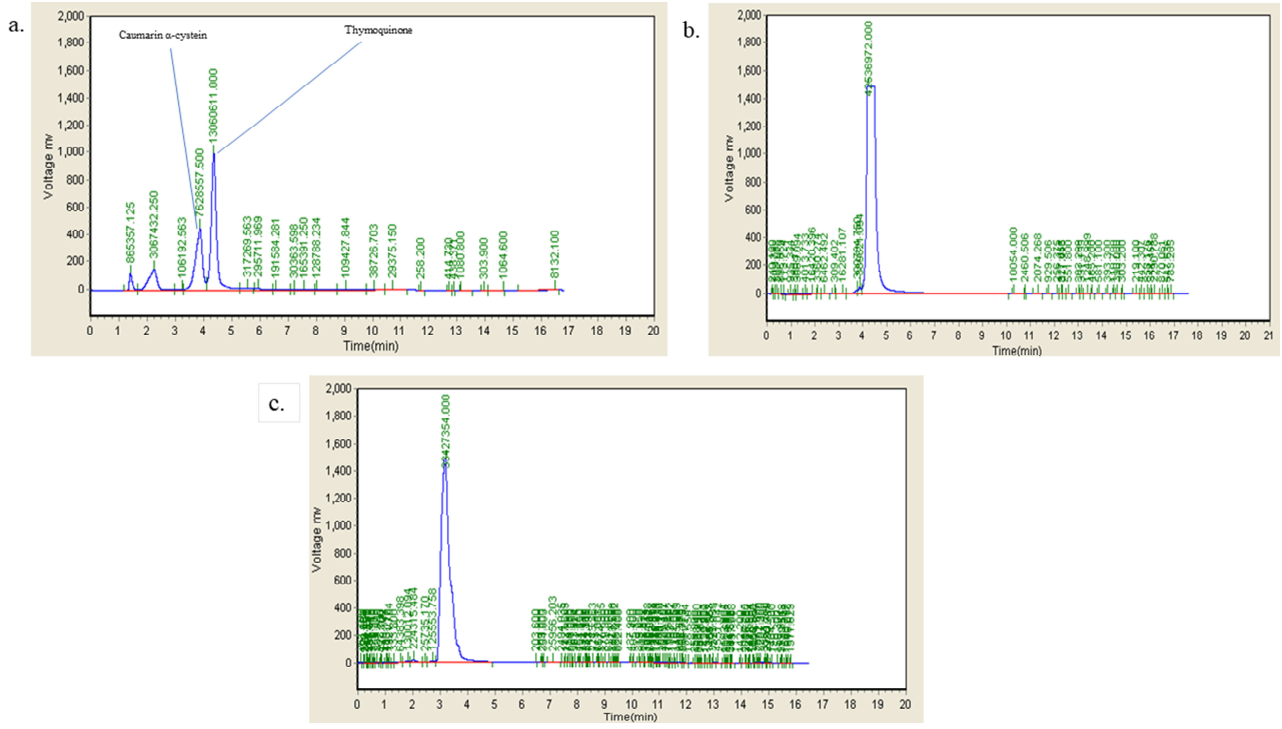


Fig. 11: HPLC fingerprint chromatogram of *Cinnamomum verum* bark extract (CvB): a. CvB b. Coumarin α-cystein, c. Thymoquinone

antidepressant and decrease the oxidative stress and chronic inflammation (Modarresi Chahardehi *et al*., 2024). Coumarins are a class of naturally occurring *O*-heterocyclic compounds and possess antifungal, antibacterial, anti-inflammatory, antioxidant, anti-cholinesterase, antidiabetic, anti-HIV, anticoagulant and anticancer effects (Rohman *et al*., 2024). Due to the presence of these compounds the CvB has a protentional benefits for the treatment of diabetes and inflammation.

Many anti-obesity and anti-diabetic drugs currently on the market have inconsistent efficacy and come with notable side effects. This has led to a growing interest in herbal and Ayurvedic formulations, traditional medicinal practices from Asia, which are recognized for their lower toxicity and minimal side effects compared to synthetic drugs. These natural formulations are gaining popularity as treatments for metabolic disorders like diabetes and obesity. *In vivo* studies have indicated that CvB contains promising anti-obesity and anti-diabetic compounds, suggesting that a tablet-based formulation of CvB could be a viable alternative to conventional allopathic medications for these conditions.

CONCLUSION

This research work concluded that *Cinnamomum verum* J. Presi (CvB) ethanolic extract of bark possesses anti-inflammatory, anti-obesity and antidiabetic potential. It can be used for long period of time for the treatment of obesity and diabetes. This conclusion is supported by the results of biochemical parameters like decreasing the serum level of lipid profile, liver enzymes and improvement in renal function.

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REFERENCES

Alrouji M, Al-Kuraishy HM, Al-Gareeb AI, Alexiou A, Papadakis M, Saad HM and Batiha GES (2023). The potential role of human islet amyloid polypeptide in type 2 diabetes mellitus and Alzheimer's diseases. *Diabetol. Metab. Syndr,* **15**: 1-16.

Alzahrani RR, Alkhulaifi MM, Al Jeraisy M, Albekairy, AM, Ali R, Alrfaei BM, Ehaideb SN, Al-Asmari AI, Qahtani SA and Halwani A (2024). Enhancing gentamicin antibacterial activity by co-encapsulation with thymoquinone in liposomal formulation. *Pharmaceutics,* **16**: 1330.

Anyasor GN, Ogunbiyi B and Akinlusi IA (2017). Antioxidant and anti-inflammatory properties of selected polyherbal preparations: Oroki herbal, Swedish bitters and Yoyo bitters. *Oxid. Antioxid. Med. Sci.,* **6**: 25-29.

Ariyanto EF, Multom NO, Berbudi A, Rohmawaty E and Sujatmiko B (2021). Efficacy and mechanism of action of *Aloe vera, Cinnamomum zeylanicum, Curcuma longa, Garcinia cambogia* and *Garcinia mangostana* extracts in lowering body weight in obesity: A literature review. *Biomed. Pharmacol. J.,* **14**: 1791-1797.

Ashraf JM, Rabbani G, Ahmad S, Hasan Q, Khan RH, Alam K and Choi I (2015). Glycation of H1 histone by 3-deoxyglucosone: Effects on protein structure and generation of different advanced glycation end products. *PLoS One,* **10**: e0130630.

Chopade AR, Somade PM and Sayyad FJ (2012). Membrane stabilizing activity and protein denaturation: A possible mechanism of action for the anti-inflammatory activity of *Phyllanthus amarus. J. Krishna Inst. Med. Sci. Univ.* **1**: 67-72.

Collins K, Hart D, Seerattan R, Reimer R and Herzog W (2018). High-fat/high-sucrose diet-induced obesity results in joint-specific development of osteoarthritis-like degeneration in a rat model. *Bone Joint Res.,* **7**: 274-281.

De Paz GA, Raggio J, Gómez-Serranillos M, Palomino O, González-Burgos E, Carretero M and Crespo A (2010). HPLC isolation of antioxidant constituents from Xanthoparmelia spp. *J. Pharm. Biomed. Anal.,* **53**: 165-171.

Ezenwaka CE, Okoye O, Esonwune C, Onuoha P, Dioka C, Osuji C, Oguejiofor C and Meludu S (2014). High prevalence of abdominal obesity increases the risk of the metabolic syndrome in Nigerian type 2 diabetes patients: using the International Diabetes Federation worldwide definition. *Metab. Syndr. Relat. Disord.,* **12**: 277-282.

Gomez-Dominguez E, Gisbert J, Moreno-Monteagudo J, Garcia-Buey L and Moreno-Otero R (2006). A pilot study of atorvastatin treatment in dyslipemid, non‐alcoholic fatty liver patients. *Aliment Pharmacol. Ther*., **23**: 1643-1647.

Gulcin I, Kaya R, Goren AC, Akincioglu H, Topal M, Bingol Z, Cetin Çakmak K, Ozturk Sarikaya SB, Durmaz L and Alwasel S (2019). Anticholinergic, antidiabetic and antioxidant activities of cinnamon (Cinnamomum verum) bark extracts: Polyphenol contents analysis by LC-MS/MS. *Int. J. Food Prop.,* **22**: 1511-1526.

Gunathilake KDPP, Ranaweera KKDS and Rupasinghe H PV (2018a). *In vitro* anti-inflammatory properties of selected green leafy vegetables. *Biomedicines,* **6**: 107-117.

Gunathilake KDPP, Ranaweera KKDS and Rupasinghe HPV (2018b). Influence of boiling, steaming and frying of selected leafy vegetables on the *in vitro* anti-

inflammation associated biological activities. *Plants,* **7**: 22-32.

Gupta Jain S, Puri S, Misra A, Gulati S and Mani K (2017). Effect of oral cinnamon intervention on metabolic profile and body composition of Asian Indians with metabolic syndrome: A randomized double-blind control trial. *Lipids Health Dis.,* **16**: 1-11.

Jain P, Soni A, Jain P and Bhawsar J (2016). Phytochemical analysis of Mentha spicata plant extract using UV-VIS, FTIR and GC/MS technique. *J. Chem. Pharm. Res.,* **8**: 1-6.

Jariyapamornkoon N, Yibchok-Anun S and Adisakwattana S (2013). Inhibition of advanced glycation end products by red grape skin extract and its antioxidant activity. *BMC Complement. Altern. Med.,* **13**: 1-9.

Kariawasam K, Pathirana R, Ratnasooriya W, Handunnetti S and Abeysekera W (2017). Phytochemical profile and *in vitro* anti-inflammatory activity of aqueous leaf extract of Sri Lankan variety of *Psidium guajava* L. *J. Pharmacogn. Phytochem.,* **6**: 22-26.

Khizar A, Rhizwania G, Zahida H, Shareef H and Taqi M (2019). *Musa paradisiaca* L. may restore pancreatic morphology and function to trigger its anti-diabetic and hypolipidemic activities in alloxon-induce diabetic rats. *Med. Aromat. Plant,* **08**(333): 1-8.

Kim JE, Kim JS, Jo MJ, Cho E, Ahn SY, Kwon YJ and Ko GJ (2022). The roles and associated mechanisms of adipokines in development of metabolic syndrome. *Molecules,* **27**: 334.

Lamichhane G, Sharma G, Sapkota B, Adhikari M, Ghimire S, Poudel P and Jung HJ (2023). Screening of antioxidant, antibacterial, anti-adipogenic and anti-inflammatory activities of five selected medicinal plants of Nepal. *J. Exp. Pharmacol,* **15**: 93-106.

Mallhi TH, Abbas K, Ali M, Qadir MI, Saleem M and Khan YH (2014). Hepatoprotective activity of methanolic extract of *Malva parviflora* against paracetamol-induced hepatotoxicity in mice. *Bangladesh J. Pharmacol.,* **9**: 342-346.

Miroliaei M, Shafaei P, Aminjafari A, Barati D and Meekins R (2017). Protection against advanced glycation end products and the mode of action of lemon balm on hemoglobin fructose-mediated glycation. *Med. Chem.,* **7**: 314-20.

Modak M, Dixit P, Londhe J, Ghaskadbi S and Devasagayam TPA (2007). Indian herbs and herbal drugs used for the treatment of diabetes. *J. Clin. Biochem. Nutr.,* **40**: 163-173.

Modarresi Chahardehi A, Ojaghi HR, Motedayyen H and Arefnezhad R (2024). Nano-based formulations of thymoquinone are new approaches for psoriasis treatment: A literature review. *Front. Immunol.*, **15**: 1416842.

Mohanty D, Padhee S, Sahoo C, Jena S, Sahoo A, Panda PC, Nayak S and Ray A (2024). Integrating network pharmacology and experimental verification to decipher the multitarget pharmacological mechanism of *Cinnamomum zeylanicum* essential oil in treating inflammation. *Heliyon*, **10**: e24120. 1-24

Munshi RP, Joshi SG and Rane BN (2014). Development of an experimental diet model in rats to study hyperlipidemia and insulin resistance, markers for coronary heart disease. *Indian J. Pharmacol.,* **46**: 270-276.

Mwalimu RJ and Packirisamy ASB (2023). Phytochemical assessment and evaluation of the anti-oxidant, anti-microbial, anti-cholesterol, and anti-diabetic activities of *Triumphetta pentandra* methanol based green leaf extract. *J. Inorg. Organomet. Polym. Mater.,* **33**: 3779-3793.

Oh J, Ahn S, Zhou X, Lim YJ, Hong S and Kim HS (2023). Effects of Cinnamon (*Cinnamomum zeylanicum*) extract on adipocyte cifferentiation in 3T3-L1 cells and lipid accumulation in mice fed a high-fat diet. *Nutrients,* **15**: 5110.

Pagliari S, Forcella M, Lonati E, Sacco G, Romaniello F, Rovellini P, Fusi P, Palestini P, Campone L and Labra M (2023). Antioxidant and anti-inflammatory effect of Cinnamon (*Cinnamomum verum* J. Presl) bark extract after *in vitro* digestion simulation. *Foods,* **12**: 452.

Ramos-González E, Bitzer-Quintero O, Ortiz G, Hernández-Cruz J and Ramírez-Jirano L (2021). Relationship between inflammation and oxidative stress and its effect on multiple sclerosis. *Neurología,* **39**: 292-301

Rohman N, Ardiansah B, Wukirsari T and Judeh Z (2024). Recent trends in the synthesis and bioactivity of coumarin, coumarin-chalcone and coumarin-triazole molecular hybrids. *Molecules,* **29**: 1026.

Sakat S, Juvekar AR and Gambhire MN (2010). *In vitro* antioxidant and anti-inflammatory activity of methanol extract of *Oxalis corniculata* Linn. *Int. J. Pharm. Pharm. Sci.,* **2**: 146-155.

Savulescu-Fiedler I, Mihalcea R, Dragosloveanu S, Scheau C, Baz RO, Caruntu A, Scheau AE, Caruntu C and Benea SN (2024). The interplay between obesity and inflammation. *Life,* **14**: 856.

Scarpa ES, Antonelli A, Balercia G, Sabatelli S, Maggi F, Caprioli G, Giacchetti G and Micucci M (2024). Antioxidant, anti-inflammatory, anti-diabetic and pro-osteogenic activities of polyphenols for the treatment of two different chronic diseases: Type 2 diabetes mellitus and osteoporosis. *Biomolecules,* 14**,** 836.

Sreejesh P, Thampi BH and Sreekumaran E (2017). Hypoglycaemic effect of glibenclamide: A critical study on the basis of creatinine and lipid peroxidation status of streptozotocin-induced diabetic rat. *Indian J. Pharm. Sci.,***79**: 768-777.

Sutariya S, Shah AA, Bajpai A, Sharma RJ, Pandhurnekar CP and Gupta A (2023). Fourier transform infrared spectroscopy (FTIR) analysis, antioxidant and anti-

inflammatory activities of leaf and fruit extracts of *Gymnosporia montana*. *Mater. Today,* **73**: 134-141.

Tupe RS, Kemse NG, Khaire AA and Shaikh SA (2017). Attenuation of glycation-induced multiple protein modifications by Indian antidiabetic plant extracts. *Pharm. Biol.,* **55**: 68-75.

Yang XQ, Yuan H, Li J, Fan JJ, Jia SH, Kou XJ and Chen N (2016). Swimming intervention mitigates HFD-induced obesity of rats through PGC-1α-irisin pathway. *Eur. Rev. Med. Pharmacol. Sci.,* **20**: 2123-2130.

Zhu L, Han J, Yuan R, Xue L and Pang W (2018). Berberine ameliorates diabetic nephropathy by inhibiting TLR4/NF-κB pathway. *Biol. Res.,* **51**: 1-12.