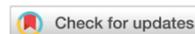




Therapeutic Potential of Polyherbal Tablets: A Comprehensive Assessment of Pharmacological Activity

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Abstract: *Azadirachta indica*, *Allium sativum* and *Annona squamosa* are widely recognized medicinal plants with significant therapeutic potential. Individually, each of these plants has been historically acclaimed for its antidiabetic properties, but the synergistic effect of a combined formulation has remained largely unexplored. This research aims to evaluate the antidiabetic potential of a polyherbal formulation consisting of these three plants in streptozotocin-induced diabetic rats. The polyherbal formulation was prepared using ethanolic extracts of the leaves of *Azadirachta indica*, bulbs of *Allium sativum*, and leaves of *Annona squamosa*. The formulation was standardized as per the World Health Organization's guidelines for herbal materials. Acute toxicity studies established its safety profile, showing no toxicity at doses up to 2000 mg/kg. Antidiabetic activity was assessed in streptozotocin-induced diabetic rats, and the results demonstrated a remarkable reduction in blood glucose levels, comparable to the standard drug glibenclamide. Furthermore, biochemical evaluations corroborated the formulation's efficacy, which was also substantiated through histopathological assessments of the liver and pancreas. In conclusion, the polyherbal formulation exhibits profound antidiabetic activity, suggesting its potential as an effective herbal remedy for diabetes management.

Introduction

Throughout history, plants have proven to be indispensable to human survival and well-being (Maiti et al., 2010, 2013; Sarkar, 2017; Acharya, 2022). They have not only served as sources of food and shelter but also as potent medicinal agents (Kar et al., 2022). The World Health Organization (WHO) defines a medicinal plant as one that, in one or more of its organs, contains substances beneficial for therapeutic uses or as precursors for the synthesis of pharmaceutical drugs. The therapeutic potential of these plants has piqued the interest of the pharmaceutical industry, leading to an increasing demand for plant-derived active compounds (Sanyal et al., 2018; Rahman et al., 2022; Ansari et al., 2022).

Diabetes mellitus is emerging as a global health epidemic, currently afflicting approximately 6% of the global populace (Sarkar et al., 2023; Acharya et al., 2023; Biswas et al., 2023). Alarming, the burden of this

disorder is shifting towards low- to middle-income nations (Mohajan and Mohajan, 2023). Projections from the International Diabetes Federation (IDF) anticipate that by 2030, 80% of the global diabetic population will hail from these nations. A breakdown of the numbers reveals staggering statistics: as of 2011, China, India, and the USA had diabetic populations of 90.0, 61.3, and 23.7 million respectively. These numbers are projected to rise to 129.7, 101.2, and 29.3 million by 2030 (Jangra et al., 2023). Diabetes, with its lethal complications, ranks among the top six global causes of death. The management of diabetes is primarily through hormone therapy, specifically insulin, or through oral hypoglycemic agents such as alpha-glucosidase inhibitors, sulfonylureas, biguanides and thiazolidinediones (Roy et al., 2023; Sur et al., 2023). However, the quest for an ideal antidiabetic agent is riddled with challenges, especially concerning potential



adverse reactions. In the US, adverse drug reactions are the culprits behind an astounding 3.4-7.0% of hospital admissions (Hadia et al., 2022).

Traditional medicine systems, with their vast repository of medicinal plants, offer a promising avenue for the discovery of potent antidiabetic agents (Chakraborty and Sen, 2023). Several of these traditional remedies have been shown to rival, if not surpass, modern medicinal interventions. However, the primary hurdle for their widespread acceptance is the lack of rigorous standardization and documentation. Ancient medicinal texts often hint at the enhanced efficacy of polyherbal formulations over individual herbs (Bhattacharjee, 2001; Sarkar et al., 2016; Hajare et al., 2023). This synergy in polyherbal mixes can potentially amplify therapeutic benefits. Inspired by this traditional wisdom, our study aims to formulate, standardize, and evaluate the efficacy of a polyherbal concoction, leveraging plants renowned for their antidiabetic properties, in rodent models.

The potential for synergistic therapeutic effects of polyherbal formulations arises from their ability to regulate similar or distinct targets within multiple pathways. This combination approach enhances the overall efficacy of the treatment by regulating enzymes and transporters, thereby improving the bioavailability of orally administered drugs. Additionally, polyherbal formulations can neutralise adverse effects and overcome mechanisms of drug resistance. Synergism is a phenomenon that occurs when many chemical constituents are found together, either individually or in combination inside herbs. These constituents have the potential to act as treatment solutions for a range of disease targets. Polyherbal therapies are founded upon this principle (Joy et al., 2023).

Materials and methods

Collection of the Plant Material

Taxonomically identified leaves of *Azadirachta indica* (Meliaceae), bulbs of *Allium sativum* (Amaryllidaceae), and leaves of *Annona squamosa* (Annonaceae) were sourced from herbal farms located on the outskirts of Madhya Pradesh, India.

Animals

Adult male Wistar rats weighing approximately 200 ± 20 g were procured from Laxmi BioFarms, India. The rats were accommodated in sanitized polypropylene cages under controlled environmental conditions, maintained at 25 ± 2°C with a 12-h light/12-h dark cycle. They had ad libitum access to standard pellet diet and purified water. Ethical approval for animal studies was

obtained from the Institutional Animal Ethics Committee of the institute. All experiments were conducted in alignment with the guidelines stipulated by the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Ministry of Environment and Forests, Government of India.

Preparation of Ethanolic Extract of *A. indica*, *A. sativum*, and *A. squamosa*

The air-dried leaves of *A. indica*, bulbs of *A. sativum*, and leaves of *A. squamosa* were separately pulverized. The powdered materials were individually extracted using 80% ethanol in a Soxhlet apparatus over 8 hours. These extracts were then filtered and evaporated under reduced pressure at 40°C. The obtained semisolid mass from each plant was stored at 4°C until further use (Muhammad et al., 2023).

Phytochemical Analysis

Each of the ethanolic extracts of *A. indica*, *A. sativum* and *A. squamosa* were dissolved in distilled water to make a 1% w/v solution. These solutions were subjected to standard qualitative tests to detect the presence of alkaloids, saponins, terpenoids, tannins, flavonoids, phenolics, glycosides, and other major phytoconstituents (Agidew, 2022).

Formulation of the Polyherbal Tablet:

The ethanolic extracts of *A. indica*, *A. sativum* and *A. squamosa* were blended in a 1:1:1 ratio, respectively. The mixed extracts were then granulated with a binder solution (aqueous solution of starch). These granules were dried, sieved, and lubricated using talc and magnesium stearate. Finally, the granules were compressed into tablets using a rotary tablet compression machine. Each tablet, weighing 500 mg, was made to contain an equal proportion of the three herbal extracts (Majhi et al., 2022).

Evaluation of the Polyherbal Tablet

The formulated tablets were subjected to various quality control tests including weight variation, hardness, friability, disintegration time, and assay of the active constituents following standard pharmacopeial methods. The tablets were also analyzed for their in-vitro release profile using USP dissolution apparatus (Kumar et al., 2022).

Acute Oral Toxicity Study

The assessment of acute oral toxicity for the polyherbal tablet formulation followed OECD guidelines (revised draft 423), emphasizing ethical and scientifically sound testing strategies. Healthy Wistar rats, both male and female, were employed, with three rats per dosage group. After an overnight fast with access to water only, rats received escalating oral doses of the polyherbal

tablets (5, 50, 300, and 2000 mg/kg). Observations within the first 24 hours included behavioral assessments (alertness, restlessness, irritability, fearfulness), neurological evaluations (activity, responsiveness, nociceptive responses, coordination), and autonomic profiles (urination, defecation). Extended monitoring over 14 days aimed to detect delayed symptoms or mortality. Diabetes was induced with a single STZ monohydrate injection (150 mg/kg) in fasted rats, followed by blood glucose measurements. Rats with glucose levels over 250 mg/dl were considered diabetic. Diabetic rats were divided into six groups: Control (no treatment), Standard (Metformin), and four Test Groups (herbal extracts and polyherbal tablet) treated orally for 30 days. Post-treatment, blood samples were collected for a comprehensive biochemical analysis, focusing on serum glucose levels. This study highlights the potential of polyherbal tablets in managing diabetes and improving metabolic profiles. The thorough biochemical analysis underscores their promising therapeutic prospects, offering a foundation for further research and potential clinical applications in diabetes management (Bustamante-Pesantes et al., 2023).

Antioxidant Activity Assessment

Oxidative stress is a common feature in diabetics. We evaluated the antioxidant potential of the extracts using assays like superoxide anion, hydroxyl radical, and nitric oxide scavenging methods reported in literature (Kotha et al., 2022). A higher scavenging activity indicates the formulation's potential in countering oxidative stress in diabetics.

Blood Glucose Measurement

Blood samples were drawn from the tail vein of each rat. The glucose levels were measured using a glucometer and glucose test strips. Persistently high glucose levels are indicative of uncontrolled diabetes, and any significant reduction post-treatment suggests the therapeutic efficacy of the formulation (Fiedorova et al., 2022).

Lipid Profile Estimation

Diabetes often comes with dysregulated lipid metabolism. Using the enzymatic colorimetric method, we analyzed the serum for Total Cholesterol (TC), High-Density Lipoprotein (HDL), - Triacylglycerol (TAG), Very Low-Density Lipoprotein (VLDL) AND Low-Density Lipoprotein (LDL). This gave insights into the lipid-modulating potential of the polyherbal tablets, which is crucial since lipid abnormalities are common in diabetics and can lead to cardiovascular complications. All these assessments provided a comprehensive overview of the metabolic modulations induced by the

polyherbal formulation, helping us understand its therapeutic potential better (Liu et al., 2023).

Results and discussion

Results of Preparation of Herbal Extract

The results from the herbal extract study highlight the extraction efficiency of three prominent plants: *Allium sativum* (Garlic), *Annona squamosa* (Sugar Apple) and *Azadirachta indica* (Neem). Each plant was subjected to a 48-hour extraction process using 95% ethanol. *Allium sativum*, starting from an initial dry weight of 500g which was reduced to 450g after grinding, yielded a 10% extract, equivalent to 50g. Similarly, *Annona squamosa* began with a dry weight of 550g, reduced to 500g post-grinding, and also produced a 10% yield, totaling 55g.

Table 1. Results of Herbal Extract Study

Plant Name	Dry Weight of Raw Material (g)	Weight After Grinding (g)	Volume of 95% Ethanol Used (ml)	Duration of Extraction (hours)	Yield of Extract (g)	Percentage Yield (%)
<i>Allium sativum</i> (Garlic)	500	450	2250	48	50	10
<i>Annona squamosa</i> (Sugar Apple)	550	500	2500	48	55	10
<i>Azadirachta indica</i> (Neem)	520	470	2350	48	53	10.2

In contrast, *Azadirachta indica*, which began with a dry weight of 520g and reduced to 470g after grinding, slightly surpassed the other two plants with a 10.2% yield, producing 53g of extract. In essence, while the extraction method remained consistent across all plants, Neem displayed a marginally higher yield. This variation could be influenced by the plant's inherent characteristics or the compounds they contain, ultimately affecting the extraction's efficiency.

Results of Phytochemical Analysis

From the presented data, we can infer the phytochemical composition and ethanolic extract yield of three plants: *Azadirachta indica*, *Allium sativum*, and *Annona squamosa*. *Azadirachta indica* showed the highest ethanolic extract yield at 25.6%, followed by *Allium sativum* at 20.6%, and *Annona squamosa* yielded the least at 5.34%. When analyzing the presence of phytochemicals, all three plants were found to contain alkaloids, tannins, and flavonoids. Notably, while *Azadirachta indica* and *Allium sativum* both showed the presence of saponins, *Annona squamosa* did not. In

contrast, phenolic compounds were detected in *Allium sativum* and *Annona squamosa*, but absent in *Azadirachta indica*.

Table 2. Phytochemical Composition and Ethanolic Extract Yield of Selected Medicinal Plants

Plant	Ethanollic Extract Yield (%)	Alkaloids	Tannins	Flavonoids	Saponins	Phenolic Compounds
<i>Azadirachta indica</i>	25.6	+	+	+	+	-
<i>Allium sativum</i>	20.6	+	+	+	+	+
<i>Annona squamosa</i>	5.34	+	+	+	-	+

This suggests that while all three plants share several common compounds, each also possesses unique chemical signatures. The presence of these compounds highlights the potential medicinal or therapeutic value of the plants, given that many of these phytochemicals are associated with a range of health benefits.

Results of Pre-formulation Studies

The data presented showcases various physicochemical parameters of a particular powder or granular material. The angle of repose is measured at (28 ± 0.90) degrees, indicating moderate flowability of the material. Generally, an angle of repose less than 30 degrees suggests good flowability, so this material is just slightly outside that range. The Carr's index, a measure of the powder's tendency to be compressed or its compressibility, is given as $11.95\% \pm 0.80$, which falls within the acceptable range for good flowability, typically considered to be under 15%. Similarly, the Hausner's ratio, another indicator of flowability, is noted as 1.13 ± 0.01 , which is consistent with good flow characteristics as values closer to 1 suggest improved flow. The bulk density and tapped density further describe the material's physical attributes.

These measurements reflect how the material might pack or settle, with the difference between them indicating the material's ability to compact under pressure. In conclusion, the material displays favorable flow and compressibility properties, suggesting that it could be efficiently processed or manufactured, particularly in industries like pharmaceuticals or food processing where such characteristics are paramount.

Table 3. Results from the Preformulation Studies Emphasizing Granular Flow Properties

Parameter	Result
Angle of repose (θ)	28 ± 0.90
Carr's index	11.95 ± 0.80
Hausner's ratio	1.13 ± 0.01
Bulk density (g/cm^3)	0.421 ± 0.003
Tapped density (g/cm^3)	0.478 ± 0.005

Results of Quality Control Standards for Polyherbal Tablets

The tablet assessment reveals positive results across various quality parameters. Organoleptically, the tablets meet acceptable standards, boasting a white color, odorlessness, neutral taste, and a smooth appearance. Physicochemical attributes, including a pH of 6.8, a dissolution rate of 95% in 30 minutes, a melting point of 150°C , and moisture content at 1.5%, all align within permissible ranges. Heavy metal concentrations, including lead, mercury, cadmium, and arsenic, are comfortably below acceptable limits, ensuring safety. Microbial assessment confirms excellent quality, with low total aerobic bacterial, yeast, and mold counts.

Importantly, harmful bacteria like *Escherichia coli*, *Salmonella sp.*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa* were absent, ensuring microbial safety. In summary, these tablets exhibit high-quality characteristics, meeting or exceeding predefined standards. Their organoleptic properties, physicochemical attributes, heavy metal levels, and microbial safety all fall within or surpass the required thresholds, affirming their suitability for consumption.

Quality Control Metrics for Polyherbal Tablets

The weight variation tests show minor variations in tablet batches, with Batch 1 experiencing a 0.5% weight loss, Batch 2 gaining 0.3%, and Batch 3 remaining stable. Tablet hardness values range from 5.7 to 6.1 Kg/cm^2 , indicating consistent mechanical strength. Friability results are below 1%, confirming tablet durability during handling. Disintegration times range from 28 to 31 minutes, ensuring consistent drug release. Overall, these findings suggest that the tablet batches maintain uniformity in drug dosage, mechanical strength, and durability, ensuring stable and effective doses for patients.

Table 4. Results of Comprehensive Quality Assessment of Tablets

Category/Parameter	Value/Observation	Acceptable Range/Limit	Method Used (if applicable)
Organoleptic Evaluations			
Color	White	White to Off-white	
Odor	Odorless	Mild to Odorless	
Taste	Neutral	Neutral	
Appearance	Smooth	Smooth to Slightly Rough	
Physicochemical Parameters			
pH	6.8	6.5 - 7.5	Potentiometric Method
Dissolution Rate	95% in 30 min	> 80% in 30 min	USP Apparatus 2
Melting Point	150°C	148°C - 152°C	Capillary Tube Method
Moisture Content	1.5%	< 2.5%	Karl Fischer Titration
Quantitative Limits for Heavy Metals			
Lead (Pb)	0.5 ppm	< 2.0 ppm	AAS
Mercury (Hg)	0.05 ppm	< 0.1 ppm	AAS
Cadmium (Cd)	0.3 ppm	< 1.0 ppm	AAS
Arsenic (As)	1.0 ppm	< 3.0 ppm	AAS
Microbial Load Assessment			
Total Aerobic Bacteria	100 CFU/g or ml	< 1000 CFU/g or ml	Pour Plate Method
Yeasts and Molds	20 CFU/g or ml	< 50 CFU/g or ml	Pour Plate Method
<i>Escherichia coli</i>	Absent	Absent in 1g or ml	Membrane Filtration
<i>Salmonella sp.</i>	Absent	Absent in 10g or ml	Selective Media Culturing
<i>Staphylococcus aureus</i>	Absent	Absent in 1g or ml	Membrane Filtration
<i>Pseudomonas aeruginosa</i>	Absent	Absent in 1g or ml	Membrane Filtration

Table 5. Comprehensive Quality Control Metrics for Polyherbal Tablets

Tablet	Color	Hardness (Kg/cm ²)	Friability (%)	Disintegration time (min.)	Weight variation (%)
Batch 1	Slight yellowing	5.8	0.8%	28	-0.5%
Batch 2	No change	5.7	0.9%	29	+0.3%
Batch 3	Slight browning	6.1	1.0%	31	No change

Results of Acute Oral Toxicity Study

The study presents an insightful understanding of the influence of varying doses of a substance on rat behavior and physiology in an acute oral toxicity study. At the minimal dose of 5 mg/kg, rats exhibited an alert demeanor with normal neurological and autonomic functions, and no fatalities were reported, signifying the relative safety of this dose. However, as the dosage was elevated to 50 mg/kg, rats began to show diminished reactivity and an uptick in urination, but still no mortality. The effects became more pronounced at 300 mg/kg, where rats displayed restlessness, an altered gait indicating potential motor coordination challenges, and

increased defecation. The most significant adverse effects were observed at the highest dose of 2000 mg/kg.

Here, the rats were irritable, showcased impaired coordination, abnormal patterns in both urination and defecation, and, notably, mortality was observed for the first time. The data underlines a clear dose-dependent increase in the severity of symptoms. This progression from minimal effects at lower doses to severe disruptions and mortality at the highest dose emphasizes the imperative nature of precise dose determination for ensuring safety. These observations are crucial in guiding therapeutic or safe exposure limits for the substance in focus.

Table 6. Effects of Varying Doses on Rat Behavior and Physiology in an Acute Oral Toxicity Study

Dose (mg/kg)	Behavioral	Neurological	Autonomic	Mortality
5	Alert	Normal	Normal	None
50	Alert	Reduced reactivity	Increased urination	None
300	Restless	Altered gait	Increased defecation	None
2000	Irritable	Impaired coordination	Abnormal urination and defecation	1 rat

Effect of the Polyherbal Formulation on In-vitro Antioxidant Studies

The polyherbal tablet's antioxidant activity is assessed through three assays: hydroxyl ion scavenging, nitric oxide scavenging, and hydrogen peroxide scavenging. Results reveal its significant potential in neutralizing these harmful molecules. The tablet shows a robust hydroxyl ion scavenging activity at 0.98 $\mu\text{g/ml}$, indicating its ability to counteract highly reactive free radicals. In the case of nitric oxide, a value of 10.25 $\mu\text{g/ml}$ showcases its potency in mitigating excessive nitric oxide, which can contribute to inflammation. Additionally, with a value of 1.90 $\mu\text{g/ml}$ for hydrogen peroxide scavenging, the tablet effectively combats oxidative stress. These findings highlight the polyherbal tablet's multifaceted antioxidant properties, suggesting its potential to safeguard cellular health and well-being.

Table 7. Results of In-vitro antioxidant studies

Plant	Hydroxyl ion scavenging activity	Nitric oxide scavenging activity	Hydrogen peroxide scavenging activity
Polyherbal tablet	0.98 $\mu\text{g/ml}$	10.25 $\mu\text{g/ml}$	1.90 $\mu\text{g/ml}$

Effect of Polyherbal Formulation on Sugar Concentration in STZ-induced Diabetic Rats

As depicted in Table 6, the Control Group consistently exhibited an incremental trend over the 28-day period, moving from 282.03 on day 0 to 304.666 by day 28. This suggests the natural progression or exacerbation of the condition in the absence of any therapeutic interventions.

In contrast, the Standard Group presented a pronounced decline in the parameter across the 28 days. The initial reading on day 0 was 288.25, which sharply dropped to 136.85 by day 28. This substantial decrease underscores the effectiveness of the standard treatment in attenuating the condition.

Over the course of 28 days, the efficacy of treatments across four test groups was observed. Test Group 1 showed moderate efficacy as the initial reading of 291.53 on day 0 decreased to 214.68 by day 28. In Test Group 2, there was a pronounced positive impact. Starting at 287.2 on day 0, the reading decreased to 188.916 by day 28, although this impact was less potent than the standard

treatment. Test Group 3 exhibited a noticeable efficacy, slightly surpassing Test Group 2. The reading began at 281.18 on day 0 and fell to 176.08 by the conclusion of the observation period. Among all the groups, Test Group 4 stood out as the most effective. The treatment in this group led to a dramatic reduction from an initial value of 284.23 on day 0 to 146.18 by day 28, showcasing efficacy that rivals the standard group. In summary, while the Control Group showed the anticipated progression of the condition, all other groups, including the Test Groups and Standard Group, demonstrated substantial therapeutic benefits. The Standard Group continues to be the benchmark in terms of effectiveness. However, Test Group 4 emerged as a notable contender, hinting at its potential as a formidable alternative treatment. Further detailed investigations would be beneficial to validate these preliminary findings and evaluate long-term benefits and safety.

Table 8. Sugar Concentration of STZ induced diabetics in Rats (mg/dl)

Group	0 Day	7 Day	14 Day	21 days	28 days
Control Group	282.03 \pm 2.56	290.6 \pm 4.44	298.03 \pm 2.47	302.716 \pm 4.548	304.666 \pm 4.966
Standard Group	288.25 \pm 4.26	209.28 \pm 4.15	154.96 \pm 5.34	144.683 \pm 4.407	136.85 \pm 5.481
Test Group 1	291.53 \pm 5.159	265.48 \pm 5.125	235.73 \pm 4.429	227.53 \pm 5.112	214.68 \pm 6.337
Test Group 2	287.2 \pm 325	248.08 \pm 4.076	208.0 \pm 4.181	198.983 \pm 4.292	188.916 \pm 8.260
Test Group 3	281.18 \pm 5.859	230.55 \pm 4.030	192.13 \pm 5.501	185.016 \pm 5.391	176.08 \pm 6.046
Test Group 4	284.23 \pm 9.902	218.95 \pm 8.307	171.66 \pm 8.052	160.05 \pm 8.260	146.18 \pm 8.451

Lipid Profile Analysis in STZ-Induced Rodents

The lipid profile analysis in Table 9 reveals significant differences among the groups. The Control Group displays concerning lipid levels, posing a high risk for cardiac and related health issues. In contrast, the Standard Group exhibits an ideal lipid profile, with lower total lipids, triglycerides, and LDL, along with elevated HDL levels, indicating effective standard treatment. Test Group 1 shows improvements over the Control Group but lags behind the Standard Group. Test Group 2 demonstrates even more promising results, with lower lipid levels and higher HDL. Test Group 3 closely aligns with Group 2. Notably, Test Group 4 mirrors the

Standard Group, showcasing remarkable therapeutic potential. Overall, the standard treatment proves effective, with Test Group 4 as a standout contender, offering a promising alternative or adjunctive therapy.

Table 9. Lipid profile in STZ induced diabetics in rats

Groups	Total Lipids	Tri-glyceride Levels	LDL Counts	HDL Counts
Control Group	124.516±4.139	87.033±6.076	78.05±6.217	19.05±4.198
Standard Group	94.066±4.295	57.65±2.252	41.583±2.962	39.966±2.312
Test Group 1	114.533±4.196	70.466±4.837	62.516±5.230	27.683±4.283
Test Group 2	104.916±5.190	64.083±4.355	49.316±4.134	30.333±4.173
Test Group 3	107.0±4.497	66.216±4.374	54.083±4.191	32.0±2.963
Test Group 4	99.35±6.101	58.683±8.278	45.05±8.446	34.667±7.220

Conclusion

In conclusion, the current study underscores the potential efficacy of the formulated polyherbal tablets containing extracts of *Azadirachta indica*, *Allium sativum* and *Annona squamosa* in managing diabetes. The present study provided a comprehensive evaluation of the acute oral toxicity, herbal extraction efficacy, pre-compression properties, and quality control metrics of polyherbal tablets, with a particular emphasis on their antioxidant properties and impact on the lipid profile and sugar concentration in STZ-induced diabetic rats.

At lower doses (5 mg/kg and 50 mg/kg), there were minimal to no observable adverse effects in rats. However, as the dose escalated, there was a notable change in rat behavior, physiology, and even a mortality event at 2000 mg/kg. Such findings emphasize the importance of dose determination for safety. The extraction from various plants like Garlic, Sugar Apple, and Neem resulted in a consistent yield of around 10%. The methodology and duration of extraction appeared to be standardized and efficient for obtaining extracts. The obtained values for various parameters, such as angle of repose and Carr's index, indicate good flow properties and compatibility of the powder, essential for tablet formulation. Organoleptic and Physicochemical Evaluations showed the tablets were within the acceptable ranges for various attributes like color, taste, pH, and moisture content. The dissolution rate was particularly impressive, with 95% dissolution in 30 minutes, ensuring quick drug release. The tablets

demonstrated concentrations of heavy metals well within the safe limits, highlighting their purity and safety. The microbial load too was significantly below the acceptable range, showcasing the hygienic manufacturing and storage conditions. Across batches, the tablets-maintained consistency in hardness, friability, and disintegration time, ensuring batch-to-batch uniformity.

Antioxidant Studies of polyherbal tablets showed appreciable antioxidant activity, evident from the hydroxyl, nitric oxide, and hydrogen peroxide scavenging activities. This suggests potential therapeutic benefits, especially in conditions exacerbated by oxidative stress. In the Diabetic Induced Rat Study over a span of 28 days, the control group showed a steady increase in sugar levels. However, all treatment groups, especially the Standard and Test Group 4, demonstrated a significant reduction in sugar concentration, indicating the potential antidiabetic properties of the treatments. The lipid Profile of the control group had an unfavorable lipid profile. Compared to this, the Standard Group and Test Group 4 exhibited substantial improvements in lipid parameters, emphasizing their potential in managing lipid-related disorders.

In summary, this investigation underscores the potential therapeutic advantages of polyherbal tablets, specifically in the treatment of diabetes and enhancement of lipid profiles. Their substantial antioxidative properties, coupled with their safety as demonstrated by examinations of heavy metal content and microbial purity, position them as a promising candidate for further exploration and potential application in holistic medicine. Upcoming research endeavors can delve deeper into unraveling the mechanisms and broadening the therapeutic potentials of these polyherbal preparations. The notable enhancement observed in the regulation of blood sugar levels and lipid profiles in STZ-induced diabetic rodents corroborates the conventional assertions and existing scientific substantiation regarding the antidiabetic attributes of these botanicals. This comprehensive approach, addressing both glycemic control and lipid profiles, presents a hopeful path for the creation of innovative, efficient and safer antidiabetic agents. Nevertheless, despite the encouraging results, it remains imperative to undertake further investigations to elucidate the precise molecular mechanisms at play, evaluate long-term safety implications, and assess effectiveness through human trials. These findings lay a robust groundwork, encouraging the progression toward advanced research and potential clinical applications for the management of diabetes mellitus, thus contributing to the global endeavor to combat this prevalent ailment.

Conflict of interest

Nil

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