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# Effects of Indigenous Saudi Herbals on Weight Control in High Fat Diet-fed STZ Induced Diabetic Rats

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***Authors' contributions***

*This work was carried out in collaboration among all authors. Author Sibghatullah Sangi performed the conceived and designed the study. Author NMA collected and analyzed the data. Authors AB and Samreen Soomro wrote the manuscript as well as an indication that all authors read and approved the manuscript for publication must be specified.*

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## ABSTRACT

**Introduction:** Obesity, a critical global issue, involves the accumulation of excessive body fat, elevating the risk of diabetes, hypertension, and other severe health conditions. This widespread concern is particularly pronounced in nations like Saudi Arabia, demanding urgent and efficient management approaches. Addressing weight control necessitates comprehensive interventions encompassing education, dietary modifications, and increased physical activity. By following healthier lifestyles and fostering a supportive environment, improvement can be made on

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healthcare systems. Collaboration between governments, healthcare professionals, and communities is pivotal to reduce obesity's impact and fostering a healthier generations.

**Methods:** Research Design and Objectives: This study aimed to fill the existing void in excessive body weight treatments by investigating viable herbal interventions that are safe, readily accessible, and economically viable. Wistar albino rats were grouped to 5 groups with 5 animals each. Diabetics were induced by intraperitoneal injection of streptozotocin for all groups except group 1. Then respective groups were fed with fat diets for 12 weeks and herbals *Zingiber officinale* (ginger), *Nigella sativa* (black seeds) and *Allium sativum* (Garlic) from $7^{th}$ to $12^{th}$ weeks along with high fat diet. Mean Body weight and Lee's obesity index were calculated for each group.

**Results and Discussion:** In the realm of herbal efficacy, a striking trend surfaces. Among the diverse materials scrutinized, one distinct name rises—Garlic (*Allium sativum*). Its prowess in diminishing both body weight and fat content stands out prominently. Across the tested spectrum, a consistent and impressive reduction in weight prevails. Particularly, Garlic asserts its dominance as a singularly remarkable performer, showcasing unparalleled effectiveness. This herbal gem not only underscores its potency but also solidifies its position as a preeminent agent for weight and fat reduction. The findings unequivocally spotlight Garlic's exceptional role in promoting healthier body composition.

**Conclusions:** Herbals as Adjunctive Therapy for Obesity The findings underscore the potential of herbal interventions, particularly Garlic, in the management of weight control. These natural remedies hold promise as adjunctive therapeutic agents. However, further rigorous human trials and animal studies with large sample size and different methodology are essential to validate their efficacy and integration into obesity / weight control treatment regimens.

*Keywords: Diabetes mellitus; obesity; Nigella sativa; Allum sativum; Zingiber officinale; Aloe Barbadensis Miller.*

## 1. INTRODUCTION

Obesity is commonly explained by applying the body mass index, a height-to-weight ratio, usually corresponding to a specific individual's fatty tissue percentage. CDC considers Obese adults to have a BMI of 30 or higher [1]. The incidence of obesity has been increasing steadily globally for the past 50 years, so much so that it has reached the extent of the pandemic [2]. Obesity poses a significant health concern due to its impact on quantitatively augmenting various health conditions, such as Type 2 diabetes mellitus, a non-alcoholic fatty liver disease, hypertension, Ischemic heart diseases, CVA, Alzheimer's disease, osteoarthritis, sleep apnea, and cancer, leading to a rise in morbidity and mortality. [3,4] Obesity is directly proportional to developing Type 2 Diabetes Mellitus. Obesity prevention and management often do not work for longer (for example, behavioral treatments targeting reduced caloric enhancing energy uptake and boosting vitality consumption). The Majority of the individuals affected by this condition do not have access to or cannot undergo bariatric surgery, either due to its unavailability or unsuitability [5]. Several causes have been identified that lead to obesity, such as Oxidative stress that primarily occurs when intake and use of calories are out of balance. Besides this, an individual's eating pattern and several other elements also have lead to obesity, which may include a sedentary lifestyle, reduced sleep, familial tendencies, and certain medications that can cause weight gain and water retention, such as steroids, antidepressants, or some anticonvulsants [6]. Although appetite is controlled by the hypothalamus, modern lifestyles and facilities also partially add to obesity. Environmental components that lead to obesity include more than required food intake, exhausting work schedules with little or no leisure time, limited availability of healthy foods in markets, readily available fast food, and insecure public places for physical activity. [7]. Some illnesses also can cause weight gain, like Hypothyroidism, i.e., a hypoactive thyroid gland that decreases biotransformation (BMR/basal metabolic rate) and causes lethargy and exhaustion. PCOS, or polycystic ovary syndrome, occurs in almost 10 percent of women of fertile age and can cause too much body hair and fertility problems. Cushing's syndrome occurs due to an overproduction of Cortisol by the supra-renal glands and is characterized by redistribution and accumulation of fat in the shoulder, face, and neck [8]. Apart from its physical disorders, obesity may also cause psychiatric disorders for many obese individuals experience depression, social isolation, and a generally low standard of life [9]. "Type 2 diabetes (T2DM) is significantly more likely to develop in those who are severely obese. The word "diabesity" was created to suggest a plausible pathophysiological connection between these disorders because of the close relationship between obesity and diabetes. The fact that many people with T2DM are also obese emphasizes the crucial role that extra body fat plays as a major risk factor. Numerous research has confirmed the connection between obesity and the harmful consequences it has on the body [10-13]. Recent research has shown that oxidative stress is a crucial link connecting obesity with issues and related impacts. Overweight people may undergo systemic oxidative stress due to several metabolic processes, such as superoxide formation by NADPH oxidases, glyceraldehyde autooxidation, activation of protein kinase C, oxidative phosphorylation, polyol, and hexosamine. Additional factors contributing to obesity include the formation of postprandial reactive oxygen species, chronic inflammation, hyperleptinemia, and insufficient antioxidant defense. At the same time, it has been suggested in recent research that adipose tissue has a vital role in the dysregulation of homeostatic mechanisms of body weight-related disorders [14]. Very few Pharmaco-therapeutic agents are accessible to address obesity concerns. The available options incorporate Lifestyle Modification [15], dietary interventions [16], increasing physical activity [17-20], and behavior therapy [21]. Bariatric surgery is widely regarded as the most drastic approach to managing obesity. and is suitable in certain circumstances when other medical disorders are present [22]. Available Pharmacological interventions for obesity include Sibutramine, a combined serotonin-norepinephrine reuptake inhibitor that is associated with marked satiety [23-25], and Orlistat, which inhibits gastric lipase that blocks the absorption of fat present in a diet [26]. These Pharmacological agents have their adverse effects. Since time unknown, Arab folks have been using different herbals for the management of obesity and associated disorders. Some studies have also been conducted in the past to investigate the effect of herbs on obesity, like Ginger, [27] Nigella sativa, [28] Garlic, [29,30]. It has been found that the majority of these herbals possess antioxidant effects, and antioxidants are known to facilitate obesity; due to these effects, a cycle is broken, which leads to a decrease in body weight and consequent improvement in overall health status [31]. However, much is required to be done to establish the role of herbals in weight reduction, especially in the presence of co-morbidity like type 2 Diabetes Mellitus.

## 2. MATERIALS AND METHODS

### 2.1 Plant Materials

The seeds for the following plants *Zingiber officinales* (ginger), *Nigella sativa* (black seeds) and *Allium sativum* (Garlic) came from both nearby markets and far-off farms. The seeds were identified and authenticated by the Head of the Faculty of Pharmacy, Northern Border University's College of Science, Saudi Arabia.

### 2.2 Animals

Thirty male Wistar albino rats, aged 8 weeks, having approximately 250 grams with a margin of error of ±10 g weight, were obtained from the university's animal house facility. The rats were kept in rooms with a constant temperature of 25°C, a humidity range of 40–70%, and a 12-hour light/dark cycle while implementing the advantage of the experiment. Every rats used in the research received the proper care at all times according to the core guidelines for caring for animals in experiments. The NBU Deanship of Scientific Study's standards regarding the handling and use of animals were additionally accepted and followed in the study plan. Every experimental animal catered for high-fat conventional dietary intake and hydration. For 4 weeks. Each day's water consumption was monitored for animals; before commencing the treatments, a weekly assessment was conducted to determine the necessary water quantity per rat.

#### 2.2.1 STZ-Induced diabetes induction

Induction of Diabetes was done for Group 1 to Group 5 by single intraperitoneal injection of streptozotocin (STZ) citrate buffer, pH 4.0, 55 mg/kg body weight [32-33]. Body weight changes were monitored at regular intervals.

Five rats were placed in each of the six categories, which were divided up among the rats as follows:

- Group 1: STZ Induced Diabetic rats in this control group were provided with a high-fat diet for 12 weeks
- Group 2: STZ-Induced Diabetic rats were fed a high-fat diet for the first six weeks,

then *Nigella Sativa* (80 mg/kg) for next 6 weeks along with high fat diet.

- Group 3: The rats were fed high fat diet for first 6 weeks then Garlic. (0.25 g / kg body weight/day) [34].
- Group 4: STZ-Induced Diabetic rats were fed a diet rich in fat for the first 6 weeks, then Ginger (100 mg/kg/rat) for next 6 weeks along with high fat diet.
- Group 5: The rats were fed high fat diet for first 6 weeks then Aloe Vera200mg/kg/day

The rats with more than 315 Lee obesity index were considered obese. After 6 weeks of high-fat diet administration, Lee's obesity index was calculated using the standard formula $\frac{\sqrt[3]{\text{bodyweight(g)}}}{\text{naso-anal length(cm)}} \times 1000$ [35].

## 3. RESULTS

There were insignificant changes in body weights among the groups from week 7 to week 12 (Table 2 and Figs. 6-7). Overall, the data regarding Serum Glucose levels suggests that the control group (G2) maintained relatively stable blood sugar levels throughout the treatment period. *Nigella Sativa* group showed a decreasing trend in blood sugar levels over time. *Allum Sativum* exhibited a temporary spike in blood sugar levels but returned to pre-treatment levels. *Zingiber officinale* showed some variability but did not significantly impact blood sugar levels (Table 3).

### 3.1 Data Analysis

The datas obtained from the study were analysed by Descriptive statistics and were presented as means ± standard deviation (SD). Compare variables among the groups, were made by a One-Way ANOVA test (Tukey), and statistical significance was considered at a P-value less than 0.05.

The data is presented as the mean, along with the standard error. Statistical significance was assessed using the One-Way ANOVA (Turkey) test with the following comparisons: 1P versus G1, 2P versus G2, 3P versus G3, 4P versus G4, and 5P versus G5.

The dataset's mean weight is 252.78, and the standard deviation is 39.56679. These values provide information about the central tendency and variability of the weights in the dataset. The plot represents the mean weights in colored bars and lines measured over 12 weeks. The extreme mean weight values and precise values are represented visually. The mean weight 1 and mean weight 3 measurements are not quite precise compared to others.

The dataset's average weight is 292.575, and the standard deviation is 32.0695. These values provide information about the central tendency and variability of the weights in the dataset. The plot represents the mean weights (in colored bars and lines) measured over 12 weeks. The

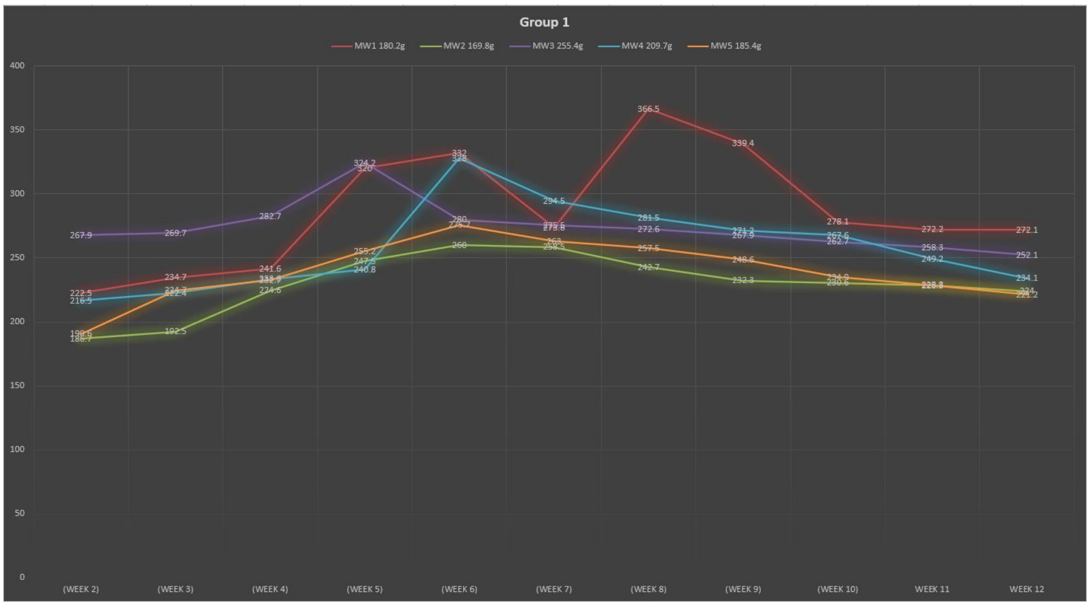


**Fig. 1. Group 1 Comparison of the body weight (grams) in different weeks**

**Table 1. Compares the body weight (measured in grams) among various groups under study**

| Groups | Week 1 | Week 2 | Week 3 | Week 4 | Week 5 | Week 6 |
|---|---|---|---|---|---|---|
| G1 (C) | 200.10±15.30 | 216.84±14.55 | 228.80±12.42 | 243.04±10.27 | 277.54±18.35 | 295.14±14.63 |
| G2 (NS) | 244.10±7.46 | 283.52±15.06 | 285.68±12.55 | 301.18±12.52 | 308.38±12.92 | 321.82±12.41 |
| G3 (AS) | 237.04±17.11 | 274.74±10.30 | 286.10±12.46 | 297.78±11.41 | 327.36±21.30 | 341.86±19.62 |
| Significance | 1P = 0.583, 2P = 1.00 | 1P = 0.181, 2P = 0.999 | 1P = 0.074, 2P = 1.000 | 1P = 0.146, 2P = 1.000 | 1P = 0.388, 2P = 0.973 | 1P = 0.313, 2P = 0.941 |
| G4 (Z0) | 256.18±18.78 | 293.38±23.15 | 320.92±14.79 | 315.40±22.15 | 329.60±15.86 | 347.54±12.49 |
| Significance | 1P = 0.168, 2P = 0.994, 3P = 0.955 | 1P = 0.037, 2P = 0.998, 3P = 0.967 | 1P = 0.001, 2P = 0.484, 3P = 0.497 | 1P = 0.026, 2P = 0.984, 3P = 0.960 | 1P = 0.341, 2P = 0.957, 3P = 1.000 | 1P = 0.205, 2P = 0.849, 3P = 1.000 |
| G5 (AV) | 255.38±18.27 | 299.94±19.09 | 300.28±17.66 | 316.56±19.83 | 335.96±17.44 | 337.12±17.72 |

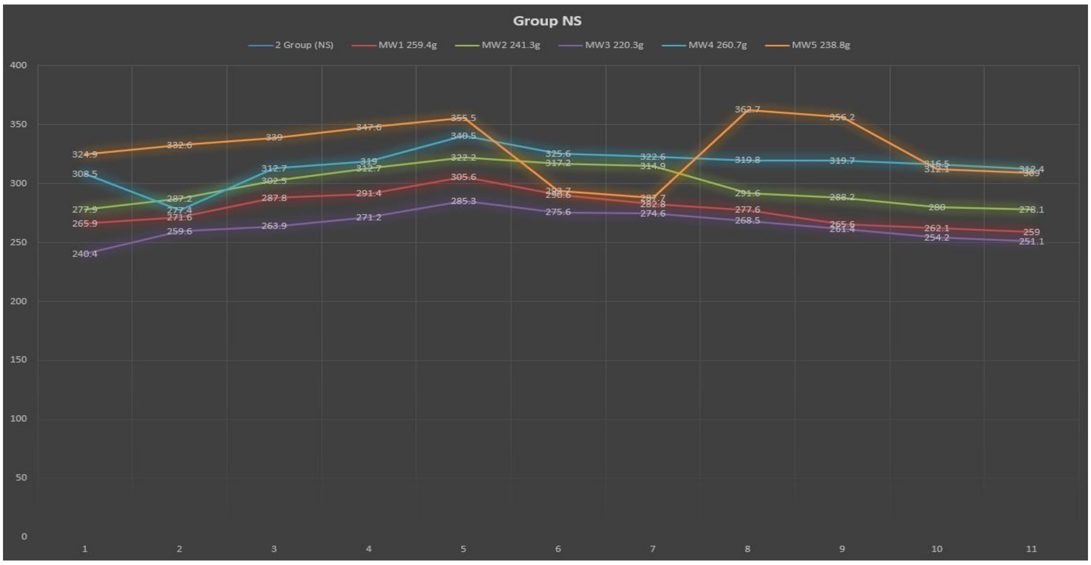


**Fig. 2. Group 2 comparison of weight of the body (grams)**

extreme mean weight values and precise values are represented visually. The mean weight 5 measurements could be more precise compared to others.

The dataset's mean weight is 276.4883, and the standard deviation is 46.17951. These values provide information about the central tendency and variability of the weights in the dataset. The plot represents the mean weights (in colored bars and lines) measured over 12 weeks. The extreme mean weight values and precise values are represented visually. The mean weight 1 and 4 measurements could be more precise than others.

The mean weight of the dataset is calculated as 295.25, and the standard deviation is 49.21555. These values provide information about the central tendency and variability of the weights in the dataset. The plot represents the mean weights (in colored bars and lines) measured over 12 weeks. The extreme mean weight values and precise values are represented visually. The mean weight 3 and mean weight measurements after week 7 could be more precise.

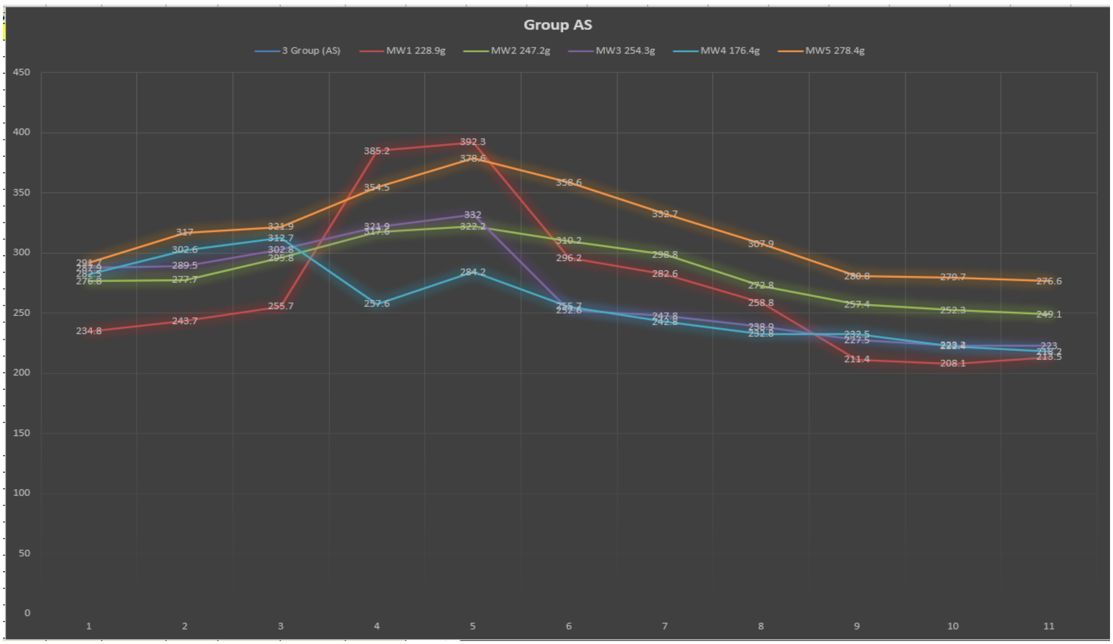


**Fig. 3. Group 3 Comparison of the body weight (grams) in 12 Weeks**

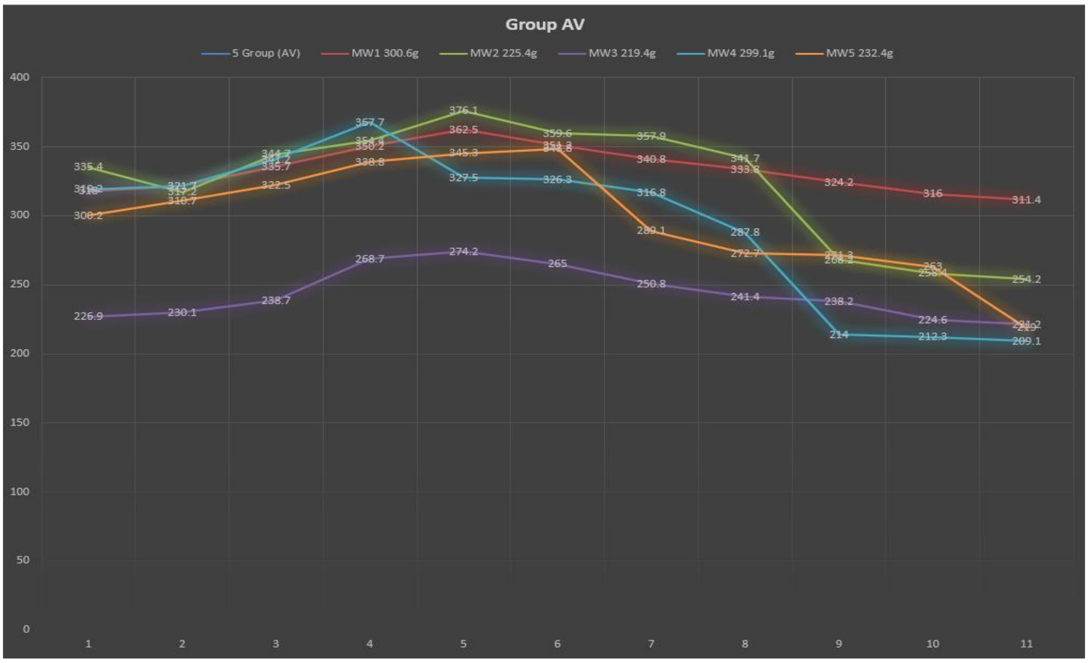


**Fig. 4. Group 4 Comparison of the body weight (grams) in 12 Weeks**

The mean weight of the dataset is calculated as 297.4433, and the standard deviation is 49.97186. These values provide information about the central tendency and variability of the weights in the dataset. The plot represents the mean weights (in colored bars and lines) measured over 12 weeks. The extreme mean weight values and precise values are represented visually. Except for mean weight measurements 3 and 4, the rest are precise but may not be accurate as mean weight measurements 1 and 5 and mean weight measurements 3 and 2 are different, precise at two points, 350 g, and 275 g.

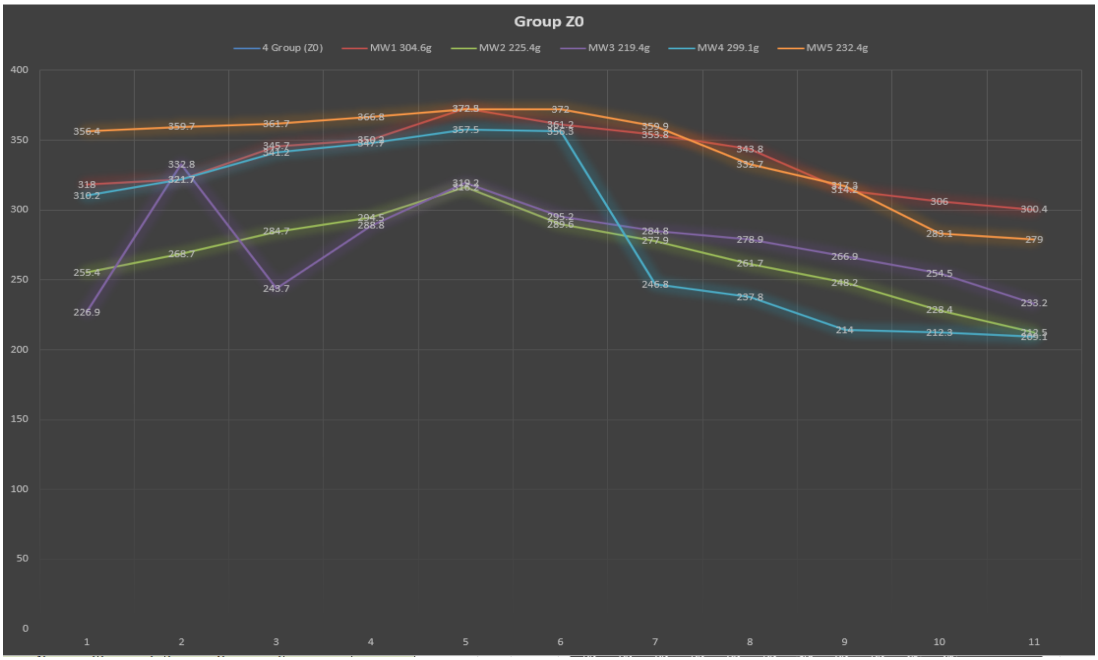


**Fig. 5. Group 5 Comparison of the body weight (grams) in 12 Weeks**

**Table 2. Comparison of the body weight (grams) in different studied groups from 7th to 12th week**

| Groups | Week- Seven | Week- Eight | Week- Nine | Week- Ten | Week- Eleven | Week- Twelve |
|---|---|---|---|---|---|---|
| G 1 ( C ) | 273.02±6.24 | 284.16±21.62 | 271.88±18.28 | 254.78±9.36 | 247.36±8.51 | 240.70±9.54 |
| G 2 (NS ) | 300.54±9.15 | 296.52±9.39 | 304.04±17.04 | 298.22±17.81 | 284.98±12.70 | 281.92±12.55 |
| Significance | 1P =0.974 | 1P =0.997 | 1P =0.775 | 1P =0.463 | 1P =0.528 | 1P =0.440 |
| G 3 ( AS ) | 294.66±19.52 | 280.94±16.66 | 262.24±13.45 | 241.92±12.21 | 237.14±12.84 | 236.08±11.86 |
| Significance | 1P=0.927, 2P=1.000 | 1P=1.000, 2P=0.991 | 1P=0.999, 2P=0.541 | 1P=0.994, 2P=0.203 | 1P=0.997, 2P=0.276 | 1P=1.000, P=0.327 |
| G 4 ( Z0 ) | 334.86±17.54 | 304.64±22.28 | 290.98±20.45 | 272.12±19.73 | 256.86±17.18 | 246.84±18.29 |
| Significance | 1P=0.104, 2P=0.656, 3P=0.497 | 1P=0.970, 2P=1.000, 3P=0.945 | 1P=0.968, 2P=0.994, 3P=0.845 | 1P=0.976, 2P=0.875, 3P=0.794 | 1P=0.998, 2P=0.787, 3P=0.941 | 1P=1.000, 2P=0.609, 3P=0.996 |
| G 5 ( AV ) | 330.18±17.20 | 311.08±19.01 | 295.48±18.85 | 263.18±18.52 | 254.86±18.09 | 242.98±18.71 |
| Significance | 1P=0.155, 2P=0.776, 3P=0.623, 4P=1.000 | 1P=0.909, 2P=0.993, 3P=0.862, 4P=1.000 | 1P=0.925, 2P=0.999, 3P=0.751, 4P=1.000 | 1P=0.999, 2P=0.679, 3P=0.943, 4P=0.999 | 1P=0.999, 2P=0.736, 3P=0.962, 4P=1.000 | 1P=1.000, 2P=0.501, 3P=1.000, 4P=1.000 |

*Data are expressed as mean +/- standard error. 1P: significance versus G1; 2P: significance versus G2; 3P: significance versus G3; 4P: significance versus G4; 5P: significance versus G5 using One Way ANOVA test (Turkey test)*

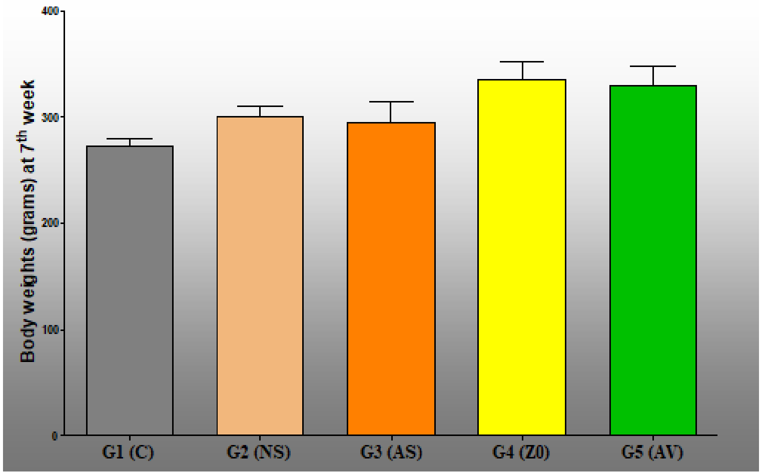


**Fig. 6. Comparison of the body weight (grams) in different studied groups at 7$^{th}$week**

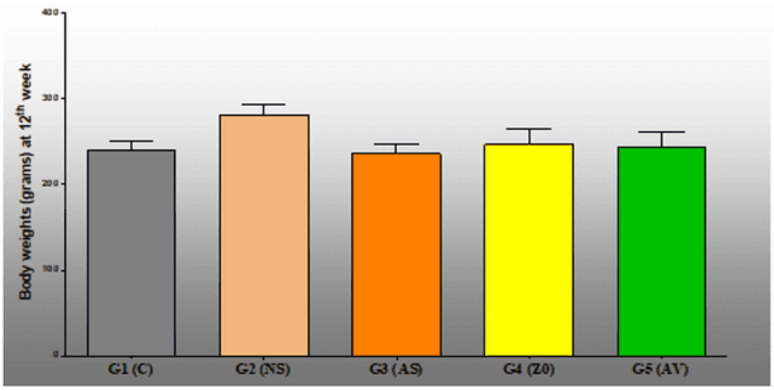


**Fig. 7. Comparison of the body weight (grams) in different studied groups in the 12$^{th}$ week**

## 4. DISCUSSION

According to a recently released report by WHO, more than one billion individuals are obese worldwide. The World Health Organization estimates that twenty-five almost 167 million people would be worse off due to obesity [36]. Increased obesity prevalence has exceptionally expanded the incidence of its complications, which affect almost every system of the body. As oxidative stress has been found responsible for all these phenomena, antioxidants have given some positive results in preventing and reducing weight in previous studies. Currently, not many drugs are available that specifically help in the reduction of weight, which is necessary for the management of many diseases like DM Type 2 and nonalcoholic fatty liver disease. It was noticed in previous studies that the herbals (*Nigella sativa*, Ginger, and Garlic which are rich in antioxidants) have the potential to reduce weight in the obese population suffering from DM and Nonalcoholic fatty liver disease [37,38]. Ginger (*Zingiber officinale*) and Garlic (*Allium sativum*) are renowned culinary spices in traditional medicine for their remarkable anti-inflammatory and antioxidant properties. Studies have indicated that these two spices can enhance the body's antioxidant defenses and exhibit anti-inflammatory effects by impeding the release of pro-inflammatory cytokines [39]. Furthermore, the spices have shown promising results in mitigating myocardial changes by promoting lipid metabolism and reducing levels of plasma C-reactive protein and inflammatory cytokines [40]. Such noteworthy biological characteristics position the ginger and Garlic as potential candidates for managing obesity and other inflammatory-related diseases. Existing evidence supports these pharmacological potentials when the extracts are administered separately. Thus, combining ginger and Garlic may yield a more potent therapeutic effect, as their secondary metabolites may act

**Table 3. Comparison of the Serum Glucose in different studied groups from day 0 to 12th week**

| Groups | Pre Treatment | Post Treatment | | | |
|---|---|---|---|---|---|
| | Day-0 | Day-14 | Day-28 | Day-56 | Day-84 |
| Control | 99±7.79 | 100.83±8.0849 | 104±9.0055 | 105.33±8.45 | 107.8±7.547 |
| *Nigella sativa* | 113±5.93 | 115.16±3.78 | 116.8±3.43 | 115.33±6.37 | 116.5±4.135 |
| *Allium sativum* | 118±2.19 | 116.16±1.72 | 113.16±3.346 | 110.6±43.75 | 103±43.57 |
| *Zingiber officinale* | 121.16±2.04 | 219±1.41 | 120.16±1.94 | 219±3.63 | 120.5±37.9098 |
| *Aloe Barbadensis Miller* | 112±12.86 | 111.16±10.028 | 110.3±8.59 | 158±51.54 | 106.5±4.76 |

*The table presents blood sugar levels for different groups over 84 days, with measurements taken at various times. The groups include a control group (G1) that received treatment. Additionally, groups are treated with Nigella Sativa, Allum Sativum, Zingiber officinale, Aloe Barbadensis Miller* synergistically, leading to enhanced therapeutic benefits. Over the past few decades, medicinal plants have gained increasing popularity compared to synthetic drugs and bariatric surgeries, primarily because of their greater accessibility and comparatively lower incidence of side effects [41]. Notably, recent research has shed light on the health benefits of various species within the Allium genus and their bioactive constituents, which encompass a wide range of advantageous properties comprising effects against obesity, diabetes, oxidation, inflammation, microorganisms, fungi, scars, and cancer. In the current study, obesity was observed for obesity in rats with diabetes. In early conducted studies on *Nigella Sativa* and Zingiber officinale, improvement in serum glucose levels and weight [39,40] has been observed. The results of our study regarding *Nigella Sativa* and *Allum sativum* adhere to the research done by Al Soom L et al. [41,42]. The reducing effects of those herbals in our study were in conformance with the earlier studies [43]. It has been suggested in previous studies that *Nigella Sativa* reduces weight by different mechanisms, such as inducing anorexia, reducing glucose absorption from the intestinal tract, reducing insulin secretion, and increasing adiponectin level [44]. The researchers have observed similar mechanisms for weight-reducing effects of *Zingiber officinale* as increased thermogenesis, decreased lipolysis, inhibition of lipogenesis, suppression of fat absorption, and decrease in appetite [45]. Many studies have found a strong relationship between oxidative stress and obesity. Many studies have found a strong relationship between oxidative stress and obesity, as well as the incidence of diabetes, obesity, cancer, cardiovascular diseases, and other health conditions. Japan is currently at the forefront of nutraceutical ingredient research, with dried rhizome of Ginger (*Zingiber officinale*) being explored for its potential anti-obesity activity. At the same time, India focuses on indigenous medicinal plants like Aconitum Heterophyllum to investigate the effects of successive plant compounds on body weight reduction [46]. The results of this study suggest that there is one common mechanism of action in the herbals used in the study, which is the antioxidant effect present in the active ingredients of the herbals.

## 5. CONCLUSION

In conclusion, these herbals can be considered for human clinical trials to prevent obesity and manage weight control in Diabetes Mellitus with comparatively cost–effective and readily available therapeutic agents. These herbals can also be used as an adjunct therapy for the treatment of obesity and associated disorders, especially Garlic (*Allum Sativum*), as it was found more effective in the management of weight in comparison to other agents used in the study. Further studies should be conducted on the active ingredients of these herbals.

## 6. SUMMARY

Obesity is a condition that leads to several pathological disorders, including Type 2 Diabetes Mellitus. There aren't many Pharmacotherapeutic agents available to manage the condition. In this study, the effects of some herbals were seen in the diabetic, high fat diet fed. It was found that herbals are effective in the reduction of weight.

## 7. STUDY LIMITATIONS

Herbal remedies for obesity and diabetes in human trials, notably Garlic. However, the study needs more robustness due to its small scale, limited dosage/formulation insight, and absence of mechanisms or safety assessment. Further rigorous clinical trials are needed to establish efficacy, safety, and optimal usage.

## ETHICAL APPROVAL

Institutional Ethical committee approval was obtained before the conducting of the study.

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## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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