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Evaluation of Antiobesity Activity of Argemone Maxicana Linn. in High Fat Diet Induced Obesity in Rats

Pratiksha Morey [a], Anjali Wankhade [b], Vivek Paithankar [c], J. V. Vyas.[d]

[a,b,c,d] *Department of Pharmacology at Vidyabharati College of Pharmacy, Amravati.*

A B S T R A C T

Obesity has become a significant global health issue with various associated ailments. Despite the increasing prevalence of obesity, there are limited pharmaceutical treatments with sustained weight loss and minimal side effects. Consequently, there is growing interest in exploring natural remedies, including herbal plants, for managing obesity. Argemone maxicana, commonly known as Mexican prickly poppy, has a long history of medicinal and dietary applications. Its various parts have been found to possess numerous beneficial properties, such as anti-obesity, hepatoprotective, and antimicrobial activities.

This study aimed to investigate the anti-obesity potential of Argemone maxicana root extract in experimentally induced obesity. The study used laboratory rats and divided them into different treatment groups, including a positive control group fed with a high-fat diet. The rats were treated with different doses of Argemone maxicana root extract for 49 days, and their body weight and blood parameters, such as cholesterol, triglycerides, and liver enzymes, were measured. Histopathological evaluation of the liver and adipose tissues was also performed.

Preliminary phytochemical screening revealed the presence of alkaloids, phenolic compounds, and proteins in Argemone maxicana root extract. The results demonstrated that treatment with Argemone maxicana root extract significantly reduced body weight compared to the positive control group. Furthermore, the extract showed beneficial effects on blood parameters related to obesity, including total cholesterol, triglycerides, HDL-C, LDL-C, VLDLC, SGOT, SGPT, total bilirubin, and blood glucose levels.

Histopathological analysis of the liver tissues revealed the recovery of normal hepatocytes in the groups treated with Argemone maxicana root extract. These findings suggest the potential anti-obesity properties of Argemone maxicana root extract and its ability to improve blood parameters associated with obesity.

In conclusion, this study highlights the potential of Argemone maxicana root extract as a natural remedy for obesity management.

Keywords: Obesity, Argemone maxicana, Mexican prickly poppy, High-fat diet.

1. INTRODUCTION

Obesity is a global health problem associated with an increased risk of various chronic diseases, including cardiovascular disorders, type 2 diabetes, and certain cancers.[1] Conventional treatments for obesity often have limitations in terms of safety and efficacy, prompting the exploration of alternative therapeutic approaches. [2] With the limitations and side effects associated with conventional anti-obesity therapies, there is a growing interest in exploring natural products as potential interventions for managing obesity. [3]

Argemone Mexicana Linn., commonly known as Mexican poppy or prickly poppy, is an herbal plant that has been traditionally used in various medicinal systems. [4] Argemone Mexicana Linn. is a member of the Papaveraceae family and is native to North and South America. It is recognized for its diverse array of bioactive compounds, including alkaloids, flavonoids, terpenoids, and phenolic compounds. [5] The Argemone Maxicana linn., also known as Mexican prickly poppy, blossoming thistle, cardo or cardosantro, is a member of the papaveraceae family and has several medical and dietary benefits [6]. These benefits are attributed to its roots, bark, leaves, flowers, fruits, and seeds. Data showed that the majority of the plant's sections have narcotic, anti-spasmodic, sedative, and analgesic, anti-Malarial, Cytotoxic, anti-Termitic, neuropharmacological, wound Healing, anti-Diabetic, antimicrobial, antibacterial, hepatoprotective properties [7]. Recent scientific investigations have suggested that Argemone Mexicana Linn. may hold promise as an effective tool in the battle against obesity. [8]

Preliminary phytochemical screening is a vital step in identifying and characterizing the bioactive compounds present in plants. [9] This study involved the extraction of bioactive compounds from Argemone Mexicana Linn. using appropriate solvents, followed by the detection of various phytochemical classes such as alkaloids, flavonoids, terpenoids, and phenolic compounds.

High-fat diet-induced obesity models have been extensively employed in obesity research due to their ability to mimic the development of obesity in humans. [10] Rats exposed to a high-fat diet exhibit characteristics similar to human obesity, including excessive adiposity, dyslipidemia, insulin resistance, and metabolic disturbances. [11]

One of the primary indicators of obesity is excessive weight gain. [12] To evaluate the impact of Argemone Mexicana Linn. on body weight regulation, body weight measurements were performed. [13] Obesity is commonly associated with excessive weight gain. To evaluate the anti-obesity potential of Argemone Mexicana Linn., an animal model or human subjects were selected, and body weight measurements were performed. These measurements enable us to assess the impact of the plant extract on body weight regulation.

This research article investigates the effect of Argemone Mexicana Linn. on obesity through parameters such as preliminary phytochemical screening, body weight measurement, and biochemical estimations, the study seeks to shed light on the anti-obesity effects of this plant. The findings from this study will contribute to the growing body of knowledge on natural products as alternative therapies for managing obesity, potentially paving the way for the development of novel anti-obesity interventions.

2. MATERIALS AND METHODS

2.1 Experimental Animal

Laboratory animals rats weighing 125–130g, obtained from the animal house of the pharmacology department at Vidyabharati College of Pharmacy in Amravati, were used in the experiment. Prior to use, each animal was acclimated to the animal housing. They are housed in cages with a 12-hour light/dark cycle. Pellets and free-flowing water were used to feed the animals. Rats were handled and cared for in compliance with the CPCSEA, a set of universally recognized standards for the treatment of animals. The Institutional Animal Committee (IAEC) of Vidyabharati College of Pharmacy, Amravati, SGB Amravati University granted permission under Registration Number-1504/PO/Re/S/11/CPCSEA and approved animal studies.

2.2 Drugs and Chemicals

Test drug ethanolic extract of Argemone maxicana (EEAM) roots is collected from Shivay Herbals and Healthcare, Bangalore. Standard drug Simvastatin (SVS) tablet manufactured in India by sun pharmaceutical ltd and brought from pharmacy store Amravati. Other chemicals like Saline solution, formalin, chloroform is also used and all are of analytical grade. All drugs and reagent were prepared immediately before use.

2.3 Collection and Preparation of Plant Extract

Following plant harvest, the roots were split apart, thoroughly cleaned in tap water, and dried in the shade for around 20 days at a controlled temperature (25 2 °C). The raw material was then pulverized, put through a sieve with a 40-mesh opening, and kept in a tightly sealed container for later use. Following drying and coarsely powdering the root, it was soxhlated in ethanol for 72 hours. In an Eyela rotary evaporator set to a temperature between 40 and 45 °C, the extracts were filtered and the solvents were evaporated to dryness under decreased pressure. Phytochemical analysis of the root extract was performed.

- Solubility Analysis

The solubility analysis of EEAM of roots has been carried out using different solvent. Extract was found to be soluble in water.

2.4 Dose Selection

i. On the basis of acute toxicity study data, it was concluded that LD50 of EEAM is up to 2000 mg/kg.

ii. Therefore, the test group were divided as 200mg/kg (low dose), 400mg/kg (high dose)[14].

2.5 High-Fat Diet Formula

HFD that consists of 58% fat, 25% protein and 17% carbohydrate, lard (13%), cholesterol (1%), vitamin, and minerals (0.6%)

2.6 Preliminary Phytochemical Screening

EEAM underwent a preliminary phytochemical screening using the procedures outlined by Khandelwal and Kokate.[15] The extract underwent phytochemical examination to identify phytochemicals like carbohydrate, alkaloids, tannins, saponins, flavonoids, triterpenoids, and steroids.[16]

2.7 Methodology

High-fat diet (HFD) induced obesity in rats is considered to be a reliable tool for the evaluation of antiobesity activity. The study comprises 5 groups with 6 animals in each group. Group 1 represented the negative control in which the animals were feed on a normal diet (NPD) and had free access to water. Group 2 represented a positive control in which the rats were feed on high-fat diet (HFD) for a period of 49 days. Group 3 represented standard control in which rats were treated with SVS (3 mg/kg, p.o). Group 4 represented test treatment in which rats were treated with the first dose of EEAM (200 mg/kg) along with high-fat diet. Group 5 represented test treatment in which rats were treated with the second dose of EEAM (400 mg/kg) along with

high-fat diet for 49 days. Various parameters like cholesterol (TC), high density lipoproteins (HDL-C), triglycerides (TG), low density lipoproteins (LDL-C), very low-density lipoproteins (VLDLC), serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), and total bilirubin were also recorded weekly. At the end of the protocol, animals were sacrificed by cervical dislocation and liver and kidney were removed to measure the change in weight and for histopathological evaluation.

2.8 Pharmacological Evaluation Parameters for Antiobesity

a. Measurement of body weight:

The body weight of the individual rat was recorded initially and at one-week intervals till the end of experiment or death of the rat.

Fig. 1 - Weekly measurement of body weight

Fig. 2 - Image at 1st week

Fig. 3 - Image at 7th week

b. Biochemical Estimations:

On the 49th day of the experiment all the animals were sacrificed by cervical dislocation, and blood samples were collected by carotid bleeding and Serum glucose, total cholesterol (TC), high density lipoproteins (HDL-C), triglycerides (TG), low density lipoproteins (LDL-C), very low-density lipoproteins (VLDLC), serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyrubic transaminase (SGPT) are observed.

c. Liver and Adipose Histopathology:

Animals are sacrificed by cervical dislocation and liver is removed to measure the change in weight and for histopathological evaluation.

2.9 Treatment protocol:

Groups	Treatment	Route of Administration
I Negative control	Normal diet	Oral
II Positive control	HFD	Oral
III Standard	HFD + SVS (3 mg/kg)	Oral
IV Treatment 1	HFD + EEAM (200mg/kg)	Oral
V Treatment 2	HFD + EEAM (400mg/kg)	Oral

Table 1: Different groups of animals and their treatment.

2.10 Statistical analysis

The data obtained from the screenings were subjected to statistical analysis following one-way ANOVA followed by Dunnett Comparison Test to assess the statistical significance of the results using GraphPad Prism-5 software.

3. RESULT

3.1 Preliminary Phytochemical Screening

Sr.No.	Natural Product	Test Performed	Inference
1	Alkaloid	Wagner's reagent	+
2	Steroids	Salkowski test	-
3	Phenolic compounds	Ferric chloride Test	+
4	Terpenoid	Salkowski Test	-
5	Carbohydrate	Molisch's Test	-
		Fehling's Test	-
6	Saponin	Soap Formation with water	-
7	Glycoside	Keller-killiani test	-
8	Protein and Free Amino Acids	Biuret Test	+

Table 2: Phytochemical Screenning.

- Indicates absence

+ Indicates presence

Phytochemical testing was carried to find out the secondary metabolites because secondary metabolites possess biological activity. The data of above table reveals that alkaloids, phenolic compounds, proteins & amino acids were present in Argemone maxicana l.

Phytochemical testing is a valuable tool for identifying and quantifying bioactive compounds present in plants. In the context of obesity, two important classes of phytochemicals, alkaloids, and phenolic compounds, have garnered attention for their potential health benefits. Alkaloids are diverse secondary metabolites that have shown anti-obesity effects by influencing lipid metabolism and appetite regulation. Phenolic compounds, on the other hand, possess antioxidant and anti-inflammatory properties, and their presence in plants has been associated with anti-adipogenic effects.

By identifying plants rich in alkaloids and phenolic compounds, scientists can explore their potential as anti-obesity agents and develop targeted interventions for managing this global health concern.

3.2 Pharmacological Evaluation Parameters for Antiobesity:

A) Measurement of body weight at 7th week:

In this study, the mea... of ... weig... 7th w... cond... assess the effects of Argemone Mexicana L. on weight progression. The objective was to ... whe... ...ant... ...a si... ...mpa... ...rats' body weight compared to a positive control group.

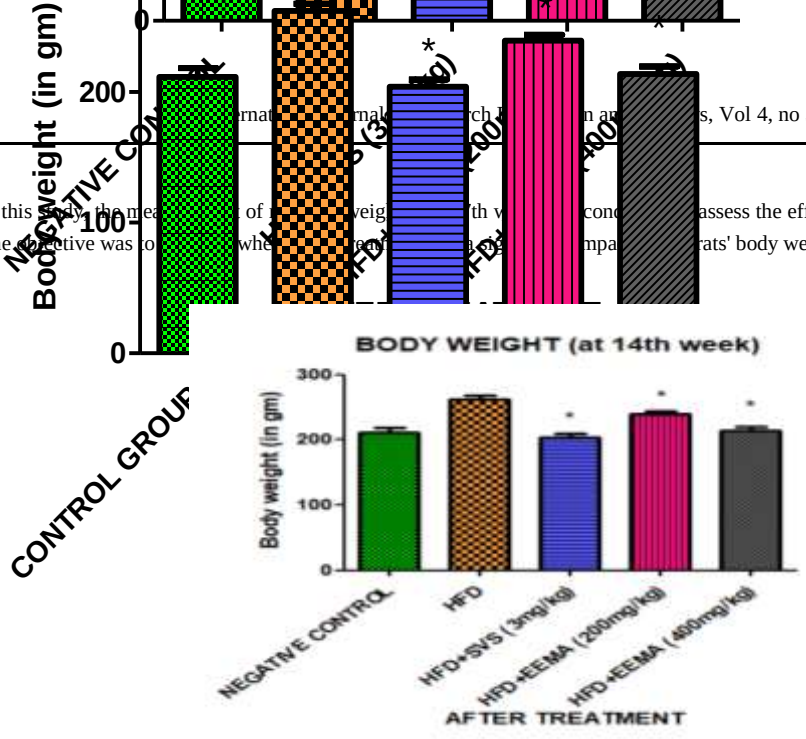


FIG 4: Final body weight at 7th week

All data are expressed as mean ± SEM for group of 6 rats in each. One-way Anova followed by Dunnett's multiple comparisons. Values are statistically Significant *P < 0.0001 for Final body weight as compared with Positive control.

The results of the statistical analysis indicated a significant difference in body weight between the treatment and control groups at the 7th week ($p < 0.0001$). This significant p-value suggested that the treatment had a notably decreased the rats' body weight compared to the positive control group. These findings highlight the potential efficacy of the Argemone Mexicana L in modulating weight progression in rats.

3.3 Measurement of Blood Parameters

Parameter	Control Group	HFD	SVS 3 mg/kg	EEAMR 200 mg/kg	EEAMR 400 mg/kg
Total cholesterol	76.83±0.9261	123.2±0.107	84.50±0.459*	102.7±0.67*	92.33±0.25*
Triglycerides	212.7±0.265	281.8±0.248	243±0.260*	267±0.303*	258.5±0.27*
HDL (mg/dL)	56.6±0.175	26.83±0.278	46.67±0.196*	32.83±0.24*	41.6±0.307*
LDL (mg/dL)	31.8±0.213	57.5±0.327	36.83±0.194*	52.5±0.216*	42.3±0.280*
VLDL (mg/dL)	22±0.141	41.67±0.186	27.5±0.242*	37.5±0.242*	33.17±0.14*
SGOT (U/L)	51.8±0.231	96±0.236	61.83±0.231*	77.33±0.13*	67.5±0.242*
SGPT (U/L)	41.17±0.194	82±0.141	48±0.20*	61.5±0.288*	52±0.236*
Total bilirubin (mg/dL)	0.5±0.04	1.9±0.08	1.17±0.9*	0.99±0.12*	0.73±0.19*
Blood glucose (mg/dL)	66.5±0.242	87.5±0.242	72.83±0.194*	82.5±0.327*	77.33±0.23*

Table 3: Effect of Argemona Maxicana on blood parameter in obese rats.

All data are expressed as mean ± SEM for group of 6 rats in each. One-way Anova followed by Dunnett's multiple comparisons. Values are statistically Significant *P <0.0001 for Blood parameter as compared with Positive control.

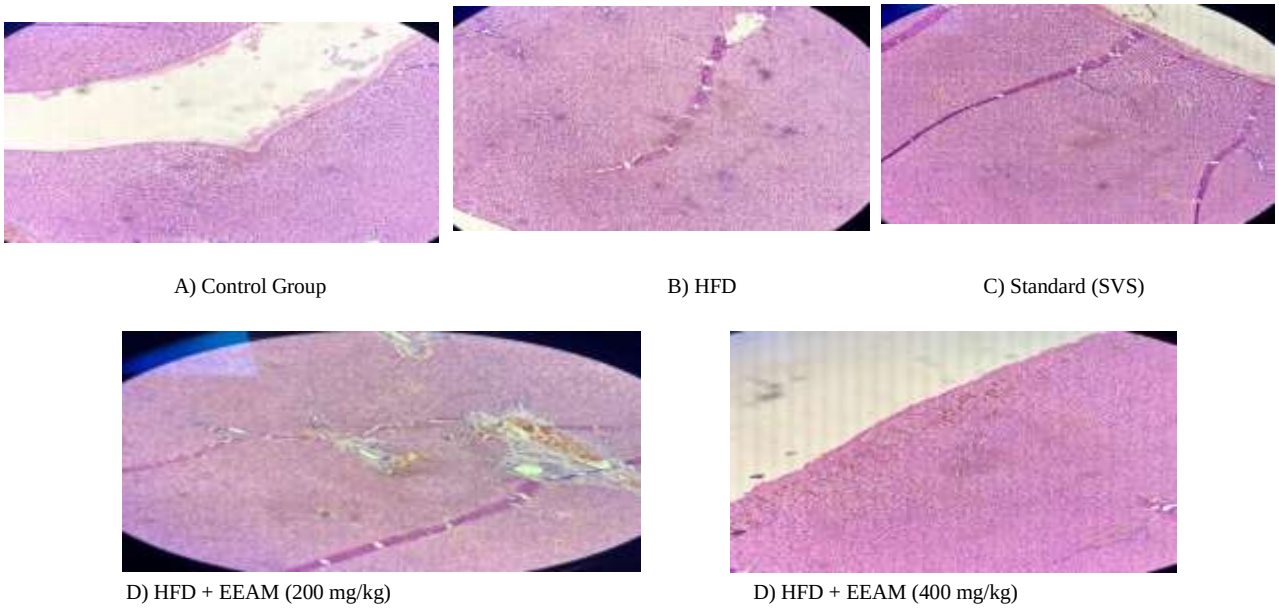
The results of the statistical analysis indicate the effect of EEAM treatment on the selected blood parameters related to obesity in rats. Depending on the outcomes, the study reports significant changes in various blood parameters, such as reductions in total cholesterol levels, triglycerides, blood glucose, etc in the treatment group compared to the positive control group.

The findings from this study contribute to understanding the potential therapeutic effects of Argemone Mexicana L on various blood parameters associated with obesity.

3.4 Histopathology of Liver in HFD Treated Rats:

A liver section of normal rat liver showed no cellular degeneration and necrosis (Figure A). Liver section of HFD treated rats showed marked vascular congestion fatty deposition and foamy degeneration of hepatocytes (Figure B), Liver section of the standard (SVS, 3 mg/kg) drug treated rats showed

normal hepatocytes and central vein but some degree of swelling (Figure C). Liver section of EEAM (200 mg/kg) treated rats showed recovered normal hepatocytes (Figure D). Liver section of EEAM (400 mg/kg) treated rats showed recovered normal hepatocytes (Figure E). (CD: cellular degeneration, VCD: vascular congestion fatty deposition, FDH: foamy degeneration of hepatocytes, CV: central vein, and N: necrosis).



A) Control Group B) HFD C) Standard (SVS)

D) HFD + EEAM (200 mg/kg) D) HFD + EEAM (400 mg/kg)

FIG 11: Histopathology of liver showing ballooning degeneration and inflammation. (CD: cellular degeneration, VCD: vascular congestion fatty deposition, FDH: foamy degeneration of hepatocytes, CV: central vein, and N: necrosis).

4. DISCUSSION

The present study investigated the effect of Argemone Mexicana L on various parameters associated with obesity, including body weight, total cholesterol, triglycerides, HDL (high-density lipoprotein), LDL (low-density lipoprotein), VLDL (very-low-density lipoprotein), SGOT (serum glutamic-oxaloacetic transaminase), SGPT (serum glutamic-pyruvic transaminase), total bilirubin, and blood glucose levels. The analysis of body weight revealed that treatment with Argemone Mexicana L had a significant effect on weight reduction. This is a promising finding, as obesity is characterized by excess body weight, and interventions aimed at weight management are crucial in combating obesity-related complications. The observed weight reduction suggests that Argemone Mexicana L may have potential anti-obesity properties. The present study aimed to investigate the effect of Argemone Mexicana L on obesity through various parameters, including histopathology and phytochemical testing, with a focus on the presence of berberine as an active phytochemical constituent.

Histopathology analysis was conducted to assess the morphological changes in adipose tissue and organs associated with obesity. The histopathological examination revealed significant improvements in the treatment group compared to the control group. In the treatment group, reductions in adipocyte size, adipose tissue inflammation, and signs of adipose tissue hypertrophy were observed. These findings indicate that Argemone Mexicana L treatment may effectively mitigate the pathological changes associated with obesity, supporting its potential as an anti-obesity agent.

Phytochemical testing was performed to identify and quantify the active constituents present in Argemone Mexicana L. The presence of berberine, a well-known alkaloid compound, was detected through phytochemical analysis. Berberine has been widely studied for its potential anti-obesity properties, including its ability to regulate lipid metabolism, improve insulin sensitivity, and modulate adipogenesis. Its presence in Argemone Mexicana L suggests that it could be a significant contributor to the observed anti-obesity effects. Berberine's mechanisms of action in obesity are multifaceted. It has been reported to activate AMP-activated protein kinase (AMPK), an enzyme involved in energy regulation, leading to increased glucose uptake, enhanced fatty acid oxidation, and inhibition of lipogenesis. Additionally, berberine has been found to modulate the expression of genes involved in lipid metabolism and adipogenesis, promoting the browning of white adipose tissue and improving metabolic parameters. The presence of berberine in Argemone Mexicana L provides a plausible explanation for the observed anti-obesity effects in this study. Its presence in the plant suggests that it could be responsible for the modulation of adipose tissue morphology and improvement in metabolic parameters observed in the treated group. It is important to note that while berberine is a known active constituent in Argemone Mexicana L, other phytochemical compounds may also contribute to the observed effects. Further phytochemical analysis could identify additional bioactive compounds that may synergistically contribute to the anti-obesity properties of Argemone Mexicana L. The findings of this study suggest that Argemone Mexicana L has potential anti-obesity effects based on histopathological improvements and the presence of berberine as an active phytochemical constituent. The observed reduction in adipose tissue hypertrophy, inflammation, and adipocyte size, along with the detection of berberine, support the use of Argemone Mexicana L as a promising natural intervention for obesity management. Further research is warranted to explore the specific mechanisms of action, optimize dosages, and evaluate long-term safety and efficacy in human subjects.

Furthermore, the study examined the impact of Argemone Mexicana L on lipid profiles, including total cholesterol, triglycerides, HDL, LDL, and VLDL levels. Elevated levels of total cholesterol, triglycerides, LDL, and VLDL are often associated with obesity and can contribute to the development of cardiovascular diseases. Conversely, increased levels of LDL, often referred to as "good" cholesterol, are beneficial for cardiovascular health. The results revealed a significant decrease in total cholesterol, triglycerides, LDL, and VLDL levels in the treatment group compared to the control group. This finding suggests that Argemone Mexicana L treatment may help improve lipid profiles, reducing the risk of cardiovascular complications associated with obesity. Additionally, an increase in HDL levels was observed, indicating a positive impact on cardiovascular health. Liver function markers, including SGOT, SGPT, and total bilirubin, were also assessed in this study. Elevated levels of these markers often indicate liver dysfunction, which can be associated with obesity-related non-alcoholic fatty liver disease (NAFLD). The results demonstrated a significant improvement in liver function markers in the treatment group, indicating a potential hepatoprotective effect of Argemone Mexicana L in the context of obesity.

Furthermore, the study examined blood glucose levels, as impaired glucose metabolism is a common feature of obesity and can lead to type 2 diabetes. The findings showed a significant reduction in blood glucose levels following Argemone Mexicana L treatment. This suggests that the treatment may have beneficial effects on glucose regulation, potentially mitigating the risk of developing diabetes in obese individuals.

Overall, the findings of this study indicate that Argemone Mexicana L has potential anti-obesity effects based on the observed reductions in body weight, total cholesterol, triglycerides, LDL, VLDL, and blood glucose levels. Additionally, the improvement in liver function markers suggests a hepatoprotective effect. These results support further exploration of Argemone Mexicana L as a potential therapeutic agent for obesity management and related metabolic disorders. However, it is important to conduct additional studies to elucidate the underlying mechanisms and determine optimal dosages and treatment durations to ensure safety and efficacy.

5. CONCLUSION

Thus, from the present study it can be concluded that the Ethanolic extract of Argemone maxicana L. is beneficial to the weight management, which supports its traditional claim. the findings of this study indicate that Argemone Mexicana L has promising anti-obesity effects. Treatment with Argemone Mexicana L resulted in significant reductions in body weight, total cholesterol, triglycerides, LDL, VLDL, and blood glucose levels. Histopathological analysis demonstrated improvements in adipose tissue morphology and reduced adipose tissue inflammation. Phytochemical testing identified the presence of alkaloid (berberine), a known active phytochemical constituent with potential anti-obesity properties. These findings support the use of Argemone Mexicana L as a potential therapeutic intervention for obesity management. Further, studies are carried out in order to determine the active principle of this plant, followed by the identification of the mechanistic approach of EEAM that helps in weight management.

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