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Research Article

Cytogenetic Effect of *Elettaria Cardimum* Alcoholic Extract Against Fluoxetine Effect on Induced Obese Rats

Amenah sabah noori[1], Huda F. Hasan[1]*

[1]*Department of Physiology, Biochemistry and Pharmacology, College of Veterinary Medicine, University of Baghdad/Iraq*

Abstract

The present study was aimed at estimating the effect of *Elettaria cardamom* attenuating Fluoxetine on cytogenetic effects on induced obese rats utilizing monosodium glutamate (MSG) . The research was conducted on 30 adult male Wistar rats which divided into 5 groups, the 1st group were treated with *Elettaria cardamomum* at dose 446.68 gm/kg orally,2nd group were treated with fluoxetine at dose 20 mg/kg orally,3rdgroup were treated with fluoxetine and *Elettaria cardamomum* together at dose (10 and 233.34 gm/kg) orally in addition to positive and negative control groups and measured the parameters for gene expression (Obese gene expression) and cytogenetic(Comet assay DNA damage, Mitotic index, chromosomal aberration). All results revealed an increase significant ($P<0.05$) in mean value in the treatment group outperformed the control group. the compound effect in rats by inducing decreasing of obese gene expression, Mitotic index, chromosomal aberration, Micro nuclei, and No DNA damage in Comet assay DNA damage. This study concluded that using both fluoxetine and *Elettaria cardamomum* together in medicine is better than using either one alone because they work better together, needless of each, are safer, and slow down or stop the development of drug resistance. This is evidenced by improvements in all parameters of this study, particularly cytogenetic alterations.

**Author for correspondence: Email: dr.hudaalgaraghuli@yahoo.com*

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Introduction

Obesity is characterized by the abnormal and excessive buildup of body fat, which can lead to various health issues. Both obesity and its antecedent, overweight, are prevalent and increasingly concerning in growing nations (Ulaiwi *et al.,* 2023; Saad, 2023). Researchers have linked various factors, including genetic predisposition and environmental influences, to the cause of obesity. Despite taking all these factors into account, interventions targeting modifiable factors, such as diet and food preservatives like monosodium glutamate, can be effective (Sabeeh, R. I., and Khudair, 2016; Al-Tamimi *et al.,* 2022; Jalili *et al.,* 2023).

(Khalil et al., 2015; Rahman *et al.,* 2017) conducted the present study to evaluate the potential benefits of *Elettaria cardamomum* extract in in obese rats supplied to a high - carbohydrate, high-fat (HCHF) diet.can use fluoxetine, a selective serotonin reuptake inhibitor, to treat major depression, obsessive behaviors, panic disorders, and bulimia. However, studies have shown that it can have negative side effects, including headache, nausea, drowsiness, diarrhea, insomnia, cardiovascular effects, sweating, decreased libido, and gene expression disorders (David *et al.,* 2009; Surour *et al.,* 2022).

Research has demonstrated a correlation between obesity and a higher occurrence of multiple types of cancer (Lin *et al.,* 2013; ALJuboury, R. A., and Al-Shawi, 2022). Obesity is known to elevate the likelihood of developing ailments such as cardiovascular disorders, diabetes, and cancer. It suggested that fat can influence genomic stability. Oxidative stress and inflammation, which frequently manifest in obesity, could cause DNA damage and hinder DNA repair pathways. The accumulation of DNA damage can lead to an enhance in the

mutation rate and affect gene expression, consequent in disruptions to cell metabolism (Najam *et al.,* 2020). Obesity-related DNA damage can accelerate cancer progression by promoting cancer cell proliferation and migration, as well as making them resistant to apoptosis. Assessing the extent of DNA destruction and/or disruptions in DNA repair mechanisms may be valuable in evaluating the hazard and preventing metabolic disorders associated with obesity and malignancies. (Abbas and Abbas, 2018; Włodarczyk and Nowicka, 2019). A recent study showed that animals that are overweight have many DNA damage problems, such as oxidized bases, single-strand breaks (SSB), and double-strand breaks (DSB). Furthermore, researchers have observed that obese subjects' lymphocytes exhibit approximately twice as much DNA damage as those of individuals with a normal weight. Furthermore, (Al-Assaf and Kadri, 2014; Włodarczyk and Nowicka, 2019) established a correlation between DNA damage and body mass index (BMI).

Methodology:

Ethical approval

All laboratory animals used in this study were approved by the scientific committee of the college of veterinary medicine, university of Baghdad in compliance with the ethical principles' guidelines on the care and use of animals in research (P.G.1299- 11/2/2024) of animal welfare.

Experimental animals:

Forty (40) male wister rat were 25-35g in weight. Were employed to carry out the study's experiment. Rats were kept in plastic cages and kept in the College of Veterinary Medicine's special housing area for two weeks so they could become acclimated to it. Distell water and common rodent food (commercial feed pellets) were also freely available. Housing conditions were kept at (25 ± 3Co) in air-conditioned rooms, where the air was regularly changed using ventilation vacuums and the light/dark cycle was 12/10. The cages' litter was replaced twice a week.

Statistical analysis:

We used the SAS (2018) program to identify the impact of various factors on the research parameters through statistical analysis. We used the T-test and least significant difference (LSD) in this study to significantly compare means, specifically through ANOVA/one-way analysis.

Experiment

We conducted this experiment to determine the effective dose (ED) and the type of pharmacodynamics interaction between cardamom seeds and fluoxetine. We will divide thirty adult rats into five member groups and administer the medication for thirty days. We will administer all treatments orally using a stomach tube:

1. The first group: six rats were left without any treatment.
2. The second group: six rats were induced obesity and treated with distilled water given orally by stomach tube.
3. The third group: six rats were induced Obesity and treated with fluoxetine at dose (20) mg/day given orally by stomach tube.
4. The fourth group: six rats were induced Obesity and treated with alcoholic extract of *cardamom* seeds at dose 446.68mg/Kg given orally by stomach tube.
5. The fifth group: six rats were induced Obesity and treated with half doses of fluoxetine (10) mg/day and extract of *cardamom* seeds half effective dose (233.34) mg/Kg given orally by stomach tube.

Parameters:

Gene expression of obese gene (Ob gene and CyPs gene) (total RNA extraction using PCR)

Gene expression primer kit/Thermo Fisher Scientific (USA)

Cytogenetic parameters (DNA comete assay, mitotic index, chromosomal aberration, Miconeucli).

Gene expression for obese gene:

a. Total RNA extraction

We applied the SpinTM whole RNA extraction (DNA-free) kit to perform the RNA extraction, adhering to the 1984 Gilbert and Church protocol.

b. Preparation of primers:

The primers utilized in this investigation were in accordance with the studies conducted by Machinal et al. in 1999 and Peinnequin et al. in 2004. The PCR protocol and parameters specified by GoTaq® 1-Step RT-qPCR for gene expression tests were followed.

Table (1): Primers of gene expression experiment.

Organism	Target gene	Primer name	5'-3'	PCR Product	Reference	Accession number
Rabbit	**Obese**	F	GACACCAAAACCCTC ATCAAG	383 bp	Machinal et al., 1999	S78586
		R	ATGTCCTGCAGAGAG CCCTG			
Rabbit	**Cyclophilin**	F	TATCTGCACTGCCAAG ACTGAGTG	127 bp	Peinnequin et al., 2004	M19533
		R	CTTCTTGCTGGTCTTG CCATTCC			

Result and discussion

gene expression

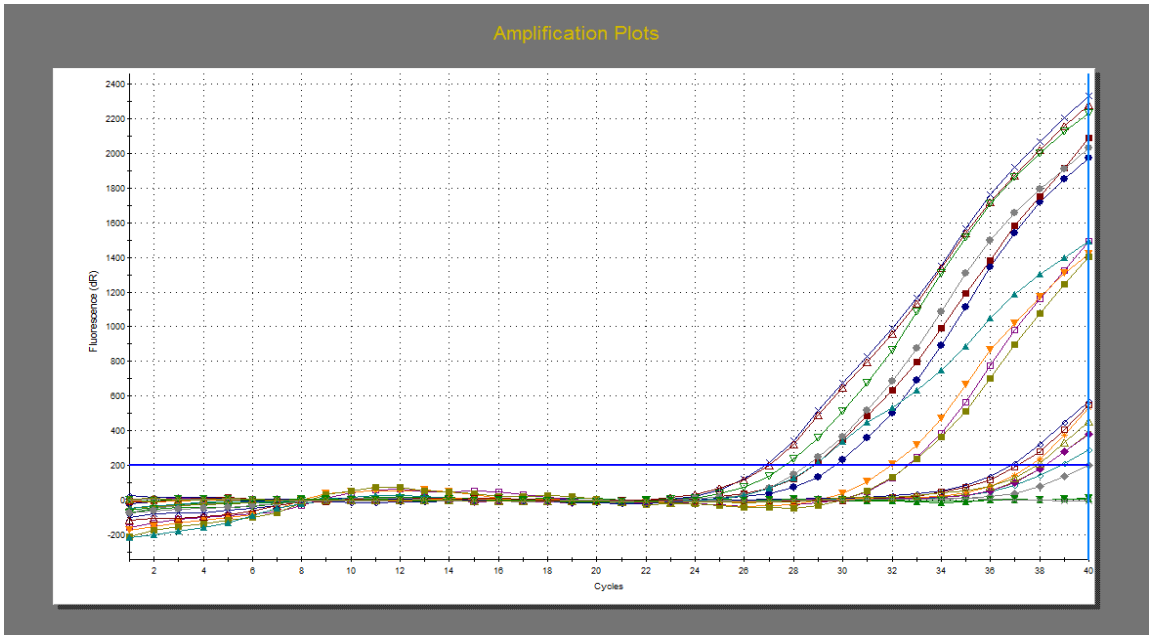
Obese gene expression

The Obese gene expression of positive control group and Obese gene expression of fluoxetine treated showed an increase significant (P≤0.05) in mean value (35.54 ±2.92) and (34.41 ±2.76) respectively compared with all other traded groups. Furthermore, Obese gene expression of *Elettaria cardamomum* treated group showed an increase significant (P≤0.05) compared with negative control group. In addition the group treated with *Elettaria cardamomum* and fluoxetine showed an increase significant (P≤0.05) in Obese gene

expression with mean value (22.49 ±1.28) compared with negative control group as, table (2).

Table 2: Effect of MSG, cardamom, fluoxetine and combination of cardamom and fluoxetine on Obese gene expression (% from control) in male rat.

Groups	Obese gene expression
C ve-	6.45 ±0.41 c
C ve+	35.54 ±2.92 a
Elettaria cardamomum	10.52 ±0.66 c
Fluoxetine	34.41 ±2.76 a
Card.+Fluox.	22.49 ±1.28 b
LSD value	11.96
Means with the different letters in same column differed significantly(P≤0.05).	



Daigram (1): Amplification Plots, *Copy of Gene expression 06.03.24.mxp.*

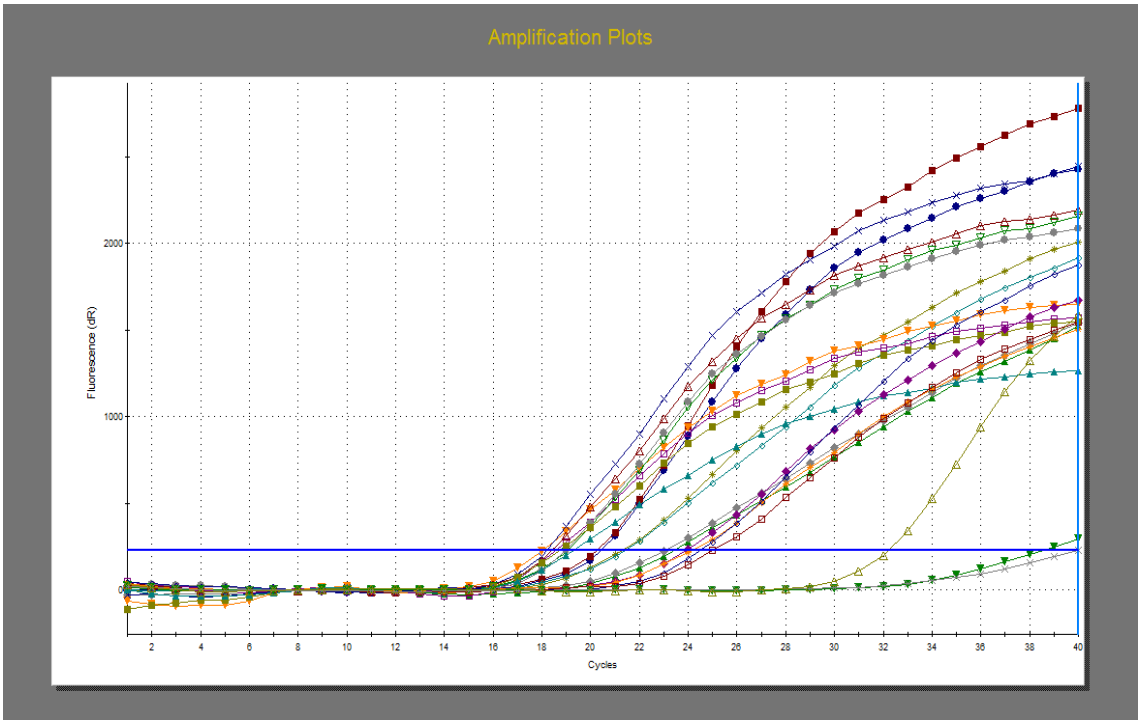


Diagram (2): Amplification Plots, *Gene expression of CypA 06.03.24.mxp*

Cytogenetic parameters:

1- **Comet assay DNA damage**

The No DNA damage% and low DNA damage% of positive control group showed a significant decrease (P≤0.05) in means values (13.66 ±0.57 and 13.58 ±0.29) respectively as compared with all other treated groups, while the medium and high DNA damage% of positive control group showed a significant increase (P≤0.05) in means values (32.57 ±.76 and 40.19 ±2.31) respectively. As well as, the No DNA damage% of *Elettaria cardamomum* treated group showed a significant increase (P≤0.05) in means values (29.60 ±3.05) compared with fluoxetine treated group with a significant decrease (P≤0.05) compared with negative control group, furthermore, low DNA damage% of *Elettaria cardamomum* treated group showed a significant increase (P≤0.05) in means values (29.60 ±3.05) compared with (45.1 ±3.67) compared with all other treated groups. In addition, the *Elettaria cardamomum* treated group showed a significant decrease (P≤0.05) in medium and high DNA damage% compared with fluoxetine treated group. While, the No DNA damage% and low DNA damage% of fluoxetine treated group showed a significant increase (P≤0.05) in means values (21.35 ±2.17 and 37.15 ±2.15) respectively as compared with group treated with both *Elettaria cardamomum* and fluoxetine, as well as, medium and high DNA damage% of fluoxetine treated group showed a significant increase (P≤0.05) in means values (10.34 ±0.72, 31.16 ±0.78) respectively as compared with combination treated group. Whereas, the animals treated with both *Elettaria cardamomum* and fluoxetine showed no significant difference (P≤0.05) in percentages of No DNA damage, low, medium and high DNA damage compared with negative control group as in table 3.

Table 3: Effect of *Elettaria cardamomum*, fluoxetine and combination of Elettaria cardamomum and fluoxetine on Comet assay DNA damage %) in male rat.

Groups	No DNA damage	Low DNA damage	Medium DNA damage	High DNA damage
C ve-	41.16 ±2.87 a	42.86 ±2.54 b	7.19 ±0.43 c	8.79 ±0.64 d
C ve+	13.66 ±0.57 d	13.58 ±0.29 d	32.57 ±.76 a	40.19 ±2.31 a
Elettaria cardamomum	29.60 ±3.05 b	45.1 ±3.67 a	6.50 ±0.38 c	18.80 ±0.39 c
Fluoxetine	21.35 ±2.17 c	37.15 ±2.15 c	10.34 ±0.72 b	31.16 ±0.78 b
Card.+Fluox.	40.75 ±2.81 a	42.55 ±2.50 b	8.85 ±0.68 c	7.85 ±0.51 d
LSD value	3.60	2.23	1.48	3.90
Means with the different letters in same column differed significantly (P≤0.05).				

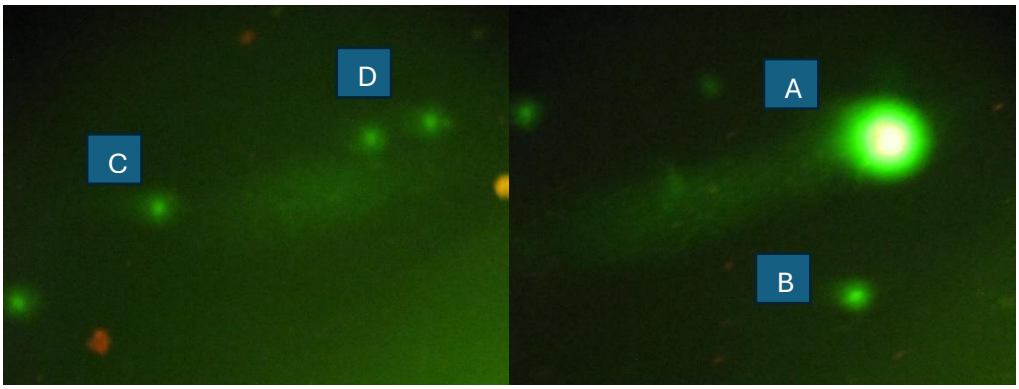


Figure 1: illustrates various degrees of damage observed in bone marrow cells. The options for comet staining are as follows: The options are: A. no comet, B. low comet, C. moderate comet, and D. high comet (Gel green Stain 100X).

2- Mitotic index

The Mitotic index of positive control group showed a significant increase (P≤0.05) in mean value (14.62 ±0.72) compared with all other treated groups. Furthermore, troponin troponin-I of *Elettaria cardamomum* treated group showed no significant (P≤0.05) in mean value (6.93 ±0.28) compared with negative control group with a significant decrease (P≤0.05) in mean value (6.61 ±0.31) compared with fluoxetine treated group with a significant increase(P≤0.05) in mean value (10.77 ±0.62). In addition the group treated with *Elettaria cardamomum* and fluoxetine showed significant increase (P≤0.05) in Mitotic index with mean value (8.5 ±0.29) compared with negative control group and *Elettaria cardamomum* treated group with a significant decrease (P≤0.05) compared with other treated groups as, table 4.

Table 4: Effect of *Elettaria cardamomum*, fluoxetine and combination of Elettaria cardamomum and fluoxetine on Mitotic index % in male rat.

Groups	Mitotic index %
C ve-	6.61 ±0.31 d
C ve+	14.62 ±0.72 a
Elettaria cardamomum	6.93 ±0.28 d
Fluoxetine	10.77 ±0.62 b
Card.+Fluox.	8.5 ±0.29 c
LSD value	2.28
Means with the different letters in same column differed significantly(P≤0.05).	

3- chromosomal aberration

The Dicentric, Acentric, Deletion and Chromosomal breakage of positive control group showed a significant increase (P≤0.05) in means values (1.27 ±0.18, 0.87 ±0.10, 0.94 ±0.08 and 1.85 ±0.021.85 ±0.02) respectively as compared with all other treated groups, while the Ring of positive control group showed no significant (P≤0.05) in means values (0.69 ±0.08) compared with fluoxetine mean value (0.60 ±0.07) while both showed a significant increase (P≤0.05) respectively as compared with all other treated groups. As well as, the Acentric of *Elettaria cardamomum* treated group showed significant decrease (P≤0.05) in means values (29.60 ±3.05) as compared with all other treated groups, furthermore, Dicentric, Deletion, Ring and Chromosomal breakage of *Elettaria cardamomum* treated group and *Elettaria cardamomum* and fluoxetine treated group and fluoxetine showed a significant decrease (P≤0.05) in means values of Acentric (0.37 ±0.06 and 0.52 ±0.04), Deletion (0.34 ±0.05 and 0.48 ±0.04), Ring (0.32±0.02 and 0.39 ±0.04) and Chromosomal breakage (0.35 ±0.06 and 0.41 ±0.03) compared with all other treated groups. In addition, While, the Dicentric and Acentric of fluoxetine treated group showed a significant increase (P≤0.05) in means values (0.89 ±0.12 and 0.53 ±0.07) respectively as compared with group treated with both *Elettaria cardamomum* and fluoxetine, as well as, Deletion, Ring and Chromosomal breakage of fluoxetine treated group showed a significant increase (P≤0.05) in means values (0.70 ±0.12, 0.60 ±0.07 and 0.54 ±0.08) respectively as compared with combination treated group. Whereas, the animals treated with both *Elettaria cardamomum* and fluoxetine showed no significant difference (P≤0.05) in percentages of Dicentric, Deletion, Ring and Chromosomal breakage compared with negative control group as in table 5.

Table 5: Effect *Elettaria cardamomum*, fluoxetine and combination of Elettaria cardamomum and fluoxetine on chromosomal aberration % in male rat.

Groups	Dicentric	Acentric	Deletion	Ring	Chromosomal breakage
C ve-	0.42 ±0.05 c	0.30 ±0.03 d	0.47 ±0.02 c	0.26 ±0.03 b	0.32 ±0.03 c
C ve+	1.27 ±0.18 a	0.87 ±0.10 a	0.94 ±0.08 a	0.69 ±0.08 a	1.85 ±0.02 a
Elettaria cardamomum	0.37 ±0.06 c	0.29 ±0.04 d	0.34 ±0.05 c	0.32±0.02 b	0.35 ±0.06 c
Fluoxetine	0.89 ±0.12 b	0.53 ±0.07 b	0.70 ±0.12 b	0.60 ±0.07 a	0.54 ±0.08 b
Card.+Fluox.	0.52 ±0.04 c	0.40 ±0.04 c	0.48 ±0.04 c	0.39 ±0.04 b	0.41 ±0.03 c
LSD value	0.35	0.11	0.21	0.19	0.13
Means with the different letters in same column differed significantly. (P≤0.05),					

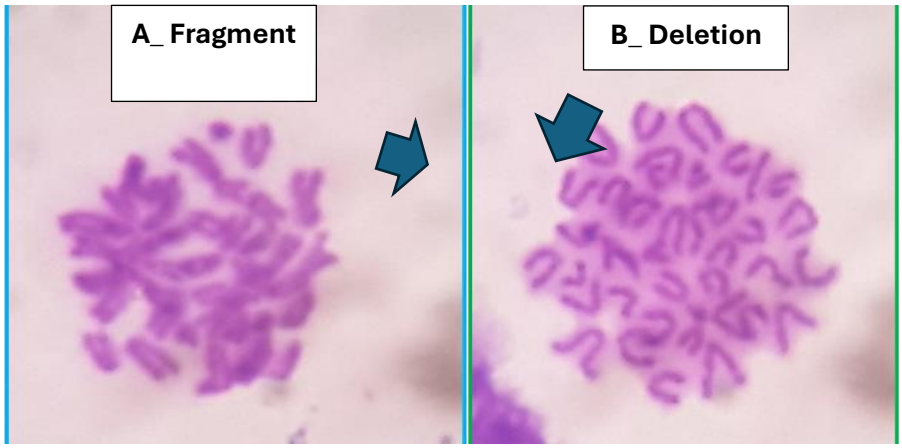


Figure 2: Cytogenetic effect of positive control group displayed the metaphase stage showed a significant presence of damaged and deleted chromosomes, the nucleus of bone marrow cells organises the genetic material into structures

known as chromosomes . A: The negative control group exhibited chromosomes that were within the usual range., as indicated by(Arrows) 100X..

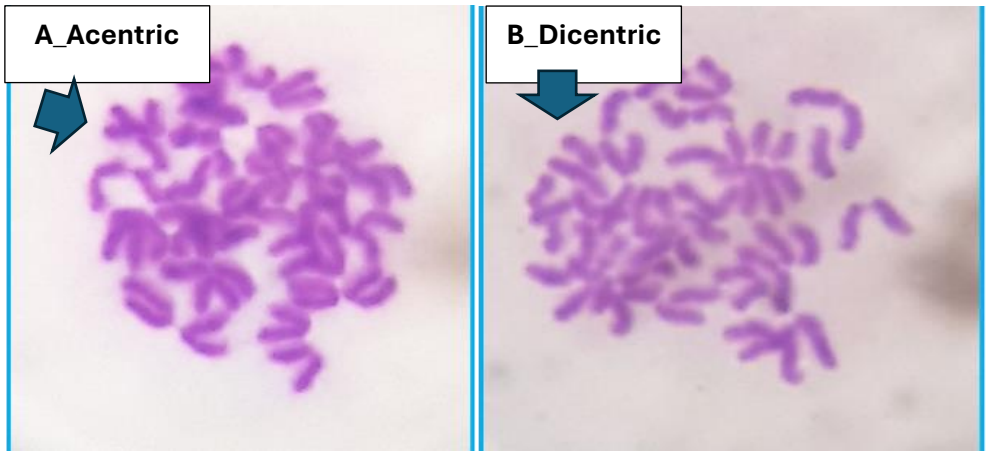


Figure 3: Metaphase chromosomes in bone marrow cell from Elettaria cardamomum treated group (G1) showed destruction chromosome A: Acentric chromosomes (Arrows) and B: Dicentric chromosomes (Arrows) 100X.

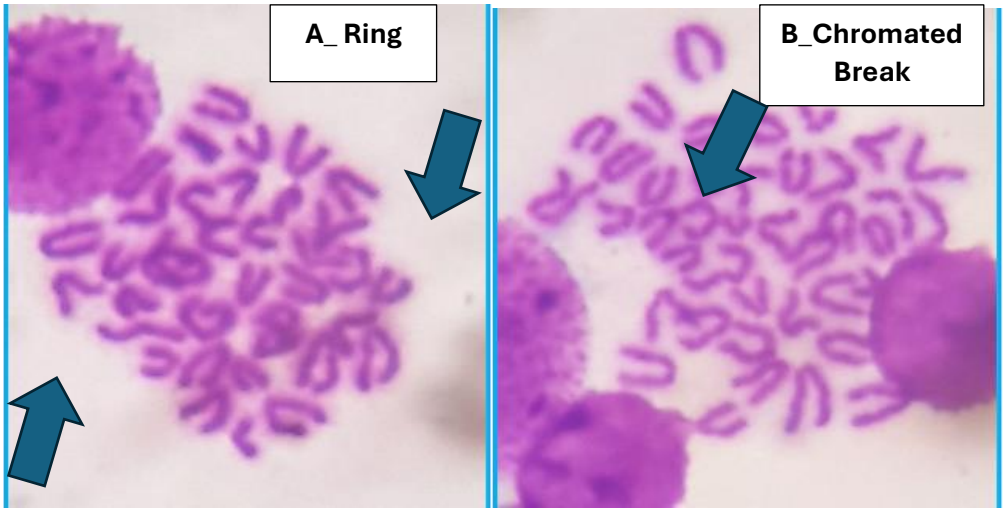


Figure 4: Metaphase chromosomes in bone marrow cell from the fluoxetine-treated group (G2) displayed the chromosomes revealed two types of damage: a ring chromosome (shown by arrows) and chromated break chromosomes. (Arrows) 100X.

4- Micro nuclei

The Micro nuclei ratio of positive control group and Micro nuclei of fluoxetine treated showed a significant increase (P≤0.05) in mean value (7.92 ±0.52) and (7.60 ±0.34) respectively compared with all other traded groups. Furthermore, Micro nuclei of, *Elettaria cardamomum* treated group showed a significant decrease(P≤0.05) in mean value (2.34 ±0.17) compared with fluoxetine treated group with a significant increase(P≤0.05) compared with negative control group. In addition the group treated with *Elettaria cardamomum* and fluoxetine showed no significant (P≤0.05) in Micro nuclei with mean value (4.69 ±0.21) compared with negative control group as, table 6.

Table 6: Effect of *Elettaria cardamomum*, fluoxetine and combination of Elettaria cardamomum and fluoxetine on Micro nuclei % in male rat.

Groups	Micro nuclei %
C ve-	2.2 ±0.07 b
C ve+	7.92 ±0.52 a
Elettaria cardamomum	2.34 ±0.17 b
Fluoxetine	7.60 ±0.34 a
Card.+Fluox.	4.69 ±0.21 b
LSD value	2.07
Means with the different letters in same column differed significantly (P≤0.05).	

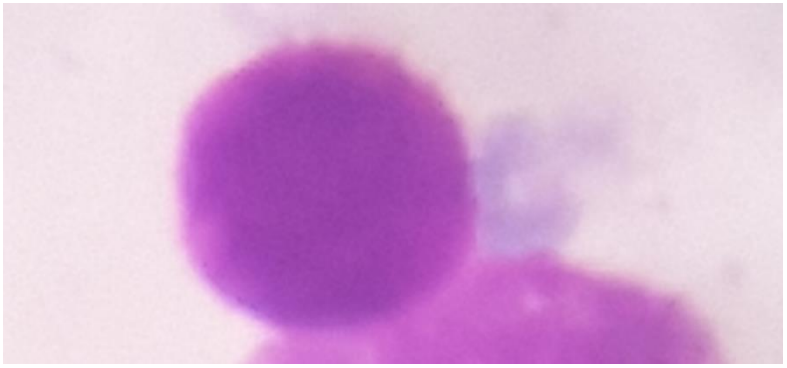


Figure 5: The bone marrow of the negative control group displayed a typical micronucleus cell.

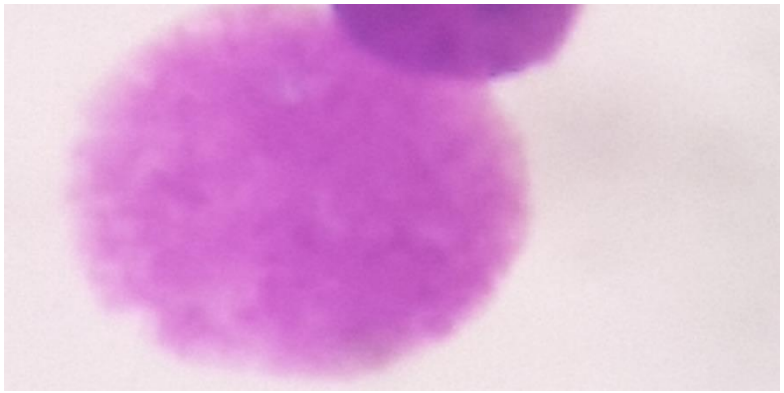


Figure 6: The image showed micronuclei (represented by arrows) in the bone marrow of rats treated with Elettaria cardamomum. Gimsa is the staining technique used, and X100 is the magnification.



Figure 7: The image depicted immature red blood cells with micronuclei (shown by arrows) in rats' bone marrow treated with fluoxetine. We used Gimsa stain and magnified the image at X100.

Discussion

Results from a study on rats explain the rise in obese gene expression in the MSG-treated group. The administration of MSG led to an increase in obese gene expression,This effect may be due to MSG's central action on the hypothalamus stimulating adipocyte enlargement. As a result, this leads to an increase in body weight and body mass index (Afifi and Abbas, 2011).

In addition, another study found that eating about the same amount of MSG as a normal person every day caused fat cells (adipocytes) to grow and increased the expression of genes related to fat metabolism and obesity (Collison *et al.,* 2009). The study showed that the expression of the obese gene in rats increased after consuming a large amount of food, possibly due to the direct effect of insulin on the adipocyte (Saladin *et al.,*1995) also reported this finding.

However, the accounts for *Elettaria cardamomum*'s contribution to reducing the expression of the obese gene in the G1 group. Research indicates that cardamom may have a role in regulating genes associated with obesity and metabolic syndrome. Some studies suggest that cardamom extracts can influence the expression of genes involved in fat metabolism, adipogenesis (the formation of fat cells), and insulin sensitivity. For instance, cardamom may help modulate the

expression of genes like PPARs (peroxisome proliferator-activated receptors), which play a critical role in fat cell differentiation and metabolism (Zhang *et al.,* 2024). The effects of green *Elettaria cardamomum* on the genes FTO, CPT1A, LEPR, LAMIN, and PPAR-γ that were linked to obesity and diabetes were better. Green *Elettaria cardamomum* is significant for lowering inflammation and enhancing insulin resistance (Ahmed, 2024). We conducted another study that linked the consumption of green *Elettaria cardamomum* to reduced levels of inflammatory markers and decreased expression of fat-related genes. *Elettaria cardamomum* stops platelets from sticking together by blocking the platelet adenosine diphosphate (ADP) P2Y12 receptor (Ahmed, 2024).

the result of fluoxetine in Obese gene expression may be attributed to Studies suggest that fluoxetine may influence the expression of genes associated with obesity and metabolism. For example, fluoxetine has been observed to affect the expression of genes involved in appetite regulation, fat storage, and energy expenditure. It may help modulate neuropeptides that play a role in hunger and satiety, such as neuropeptide Y (NPY) and pro-opiomelanocortin (POMC) (Grzesiuk *et al.,* 2023).

Before, scientists found that giving rats 4000 mg/kg of MSG caused the creation of MNPCEs, which were micro-nucleated polychromatic erythrocytes. This probably happened because the compound lowered the amount of reduced glutathione (GSH), which in turn lowered the functions of superoxide dismutase and catalase in many organs, such as the brain, liver, kidneys, and bone marrow. Researchers (Farombi *et al.,* 2006 and Proudlock, 2016) found that reactive oxygen species (ROS) and different compounds like hydrogen peroxide, hydroxyl radicals, singlet oxygen, and peroxynitrite may had a big effect on the ageing process, as well as on the making of mutations and cancer. These compounds specifically affect DNA and bone marrow, which were two vital tissues in the body.

Furthermore, a recent study discovered that MSG caused genotoxicity and cytotoxicity in animal neuronal cells, DNA breakage in hepatocytes, and the formation of micronuclei in bone marrow tissue. The liver performs various functions, such as detoxification and metabolism. It was plausible that hazardous chemicals and their metabolites could impact the liver (Shah *et al.,* 2019). Another review (Hoffelder *et al.,* 2004) found that micronuclei could also form when chromosomal material breaks apart during telophase, resulting in the generation, stretching, and subsequent breaking of nucleoplasmic bridges.

The higher number of chromosomal abnormalities seen in the MSG-treated group was similar to what (Adeyemo and Farinmade , 2013) found when they gave MSG to animals and recorded a variety of chromosomal abnormalities that changed with dose. The suppressive impact of MSG on the metaphase and anaphase phases of cellular division, which heightens toxicity, may account for this. Additionally, the presence of abnormal chromosomes indicated a potential for abnormal cell division, highlighting the risk of having an abnormal number of chromosomes, also known as aneuploidy. Finally, MSG's ability to impede spindle development may result in defects such as aneuploidy, asymmetric distribution, dicentric chromosomes , deletions, and chromosomal bridges during anaphase. Furthermore, (Mosallam, 2020) referenced a study that discovered MSG's cytotoxic and genotoxic effects on root tip cells. The study attributed these effects to the production of free radicals and the reduction of antioxidants.

Elettaria cardamomum was thought to stop platelets from activating and clumping together and from making free radicals by attaching to a platelet adenosine diphosphate (ADP) P2Y12 purinergic receptor. This may be the reason for its beneficial protective effect on cytogenetic damage (Heydarian *et al.,* 2024). In addition, *Elettaria cardamomum* possesses anti-inflammatory properties that could be helped in reducing apoptotic consequences. It had a strong protective effect on cells by controlling the expression of the Bcl gene family. This stops the Bcl gene family may be caused cytogenetic damage (Azgomi *et al.,* 2024). In current study could be utilised the therapeutic properties of *Elettaria cardamomum* to mitigate obesity-related issues and counteract the adverse effects of MSG. Furthermore, study by Ampuero *et al.,* (2024) suggested that the antioxidant, anti-inflammatory, and potent antioxidant properties of fluoxetine had anti-carcinogenic properties. Furthermore, fluoxetine's ability to alter interleukins, tumor necrosis factor, and cyclooxygenase-2 may helped explain how it prevented more cytogenetic damage.

Furthermore, (Saini *et al.,* 2018) hypothesized that fluoxetine effectively inhibited the development of micronuclei by reducing reactive oxygen species (ROS) and depleting glutathione (GSH) levels. Fluoxetine had the potential to not only provided therapeutic benefits but also to prevent the excessive production of free radicals. This was particularly important for obese patients and individuals who consumed MSG, as MSG could be lead to significant cellular damage, such as DNA oxidation, when it interacted with macromolecules within cells (Correia *et al.,* 2023).

The combination of Fluoxetine and *Elettaria cardamomum* had a more significant effect than using a single treatment alone in terms of reducing the required dosage and toxicity. This could potentially explained the notable improvements in cytogenetics observed in the G3 combination treatment group.

an increase in the level of Mitotic index by MSG and Fluoxetine treated groups and a decrease in the level of Mitotic index in cardamom and the compound MSG treated group may be attributed to MSG lead to increasing the mitotic activity and reducing the chromosomal aberration with micronucleus. In certain cell cultures, MSG can act as a nutrient that supports cellular metabolism. By providing essential amino acids, it may enhance the overall growth conditions, leading to an increased mitotic index (Taj-Al-Deen *et al.,* 2006). While the effect of Fluoxetine perhaps due to it caused damage in DNA tissue of liver which is give clear explanation about enantiomer-and stereoselective aspects of fluoxetine by its carbon center in its structure , the current result agreed with (Micheli *et al.,* 2018) who also examined the cytogenetic effect of fluoxetine in mice and showed defect in mitotic index in bone marrow compared with control group other study recoreded by Cavalcanti *et al., (*2022) revealed the effect of fluoxetine on mitotically dividing bone marrow cells

while the effect of Elettaria cardamomum in decreasing mitotic index may be attributed to Cytotoxic Effects, Some studies suggest that cardamom has cytotoxic properties that can induce

apoptosis (programmed cell death) in certain cancer cells, thereby lowering the mitotic index. Addation to Antioxidant Properties: Cardamom contains antioxidants that can reduce oxidative stress, potentially affecting cell division and leading to reduced mitotic activity (Ali *et al.,* 2020).

The effect of MSG on chromosomal aberration may be attributed to Genotoxicity, Some studies suggest that high concentrations of MSG may exhibit genotoxic effects, leading to structural changes in chromosomes and increased frequency of aberrations, and attributed to oxidative Stress, MSG can induce oxidative stress, which may damage DNA and contribute to chromosomal abnormalities (Okus *et al.,* 2024). the result of fluoxetine in on chromosomal aberration may be attributed to Genotoxic Potential, Some studies suggest that fluoxetine can induce genotoxic effects, potentially leading to structural chromosomal abnormalities, also Oxidative Stress, Fluoxetine may increase oxidative stress in cells, which can cause DNA damage and contribute to chromosomal aberrations (Öz *et al.,* 2024).

Unfortunately, fluoxetine treatment in living things has been shown in several studies to have deleterious effects on DNA and cells. (Cavalcanti *et al.,* 2022) noted that these consequences were manifested as chromosomal anomalies, exchanges between identical chromatids, and DNA fragmentation.

The effect of Elettaria cardamomum extract on chromosomal aberration may be attributed to Cytotoxicity, At high concentrations, cardamom may have cytotoxic effects that could lead to cell death rather than chromosomal damage, potentially reducing the number of cells available for analysis, also to Antioxidant Activity, Cardamom contains compounds that exhibit antioxidant properties, which can help reduce oxidative stress and potentially protect against DNA damage, thereby decreasing the likelihood of chromosomal aberrations (Issa et al., 2020).

The effect of MSG on Micro nuclei may be attributed to Some animal studies suggest that high doses of MSG can lead to an increase in micro-nuclei formation, indicating potential genetic damage (Barber *et al.,* 2023) the result of fluoxetine in on Micro nuclei may be attributed to Some studies suggest that fluoxetine may influence cellular processes related to DNA damage and repair. The formation of micro-nuclei can be an indicator of chromosomal instability and genetic damage, which may arise from various factors, including drug exposure. Research has shown varying results; some studies indicate that fluoxetine may increase the frequency of micro-nuclei formation in certain cell types, while others suggest that it may have protective effects against DNA damage (Ramakrishnan and Neducheziyean, 2021). The effect of Elettaria cardamomum extract on Micro nuclei may be attributed to Some studies have suggested that cardamom extracts may reduce the frequency of micro-nuclei formation in certain experimental models, potentially due to their antioxidant activity (Orozco-Hernández *et al.,* 2023; Delgadillo-Puga *et al.,* 2023).

The researchers discovered that cardamom greatly boosted the production of micronuclei in rats' bone marrow cells. Furthermore, the study discovered that fluoxetine could disrupted genes and created comparable levels of cytogenetic damage in adult male rats' liver, testis, and bone marrow. Comet and micronucleus tests revealed the existence of micronuclei as well as DNA fragmentation (Vijitkul *et al.,* 2022).

Conclusion

This study concluded the compound had a positive effect from a genetic perspective, unlike the effect of fluoxetine and MSG, which had a negative effect. Using both fluoxetine and Elettaria cardamomum together in medicine was better than using either one alone because they work better together, needless of each, were safer, and slow down or stop the development of drug resistance. This was evidenced by improvements in all parameters of this study, particularly cytogenetic alterations.

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NOVELTY STATEMENT

The study's novelty lies in its focus on the physiologically active compounds of Elettaria cardamomum and fluoxetine, which may serve as treatments for obesity. This is very important because there aren't many easily accessible, safe, and effective medicines for conditions related to obesity, especially when you consider the risks of other weight loss treatments. This means that we need to look for other therapeutic sources.

AUTHORS CONTRIBUTION

Each of these authors made an equal contribution to this research.

Conflict of interest

The authors have disclosed no conflicts of interest.

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