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Potential Impacts of Dried Green *Coleus forskolin* Leaves on Changes of Body and Liver Weight, Glucose and Body Temperature, Serum Profiles in Mice

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ABSTRACT

Background: Forskolin, an active compound extracted from the *Coleus forskohlii* plant, has a wide range of potential functions including losses of body weight, improves diabetes and improves cardiovascular health.

Methods: Thirty sex albino mice, growing and adult males and females were classified into two groups; control group (G1) fed basal control diet versus *C. forskolin* group fed basal control diet containing *C. forskolin* leaves (G2; 1.5%) for four weeks. Changes of body and liver weight were recorded. Rectal temperature and glucose values were determined. In addition, blood samples were collected and were subjected for serum biochemistry analysis.

Result: The results indicated that *C. forskolin* caused significant decrease (P<0.05) in body weight and glucose values in addition to significant increase (P<0.05) in rectal temperature. In addition, serum biochemistry parameters (total protein, blood urea nitrogen, creatinine, aspartate aminotransferase and alanine transferases, lactate dehydrogenase) were changed due to *C. forskolin* compared to control diet. It could be concluded that 1.5% *C. forskolin* supplementation modulates thermo-tolerance responses, blood glucose indices and serum metabolites.

Key words: Biochemistry, Body weight, *Coleus forskohlii*, Glucose, Liver.

INTRODUCTION

Coleus forskohlii, termed Avyurveda, is an Indian-origin medicinal plant cultivated in India, Nepal, Sri Lanka, Myanmar and parts of eastern Africa (Tung *et al.,* 2021). It is also cultivated in southern and western regions of KSA where it grows in mountainous areas. There is an increasing commercial demand of *C. forskohlii* plant from industries for dietary supplements, food, beverages, pharmaceuticals and cosmetics usages (Roshni and Rekha 2024). The *C. forskohlii* plant has recently gained popularity for production of forskolin compound (Mitra *et al.,* 2020; Kundur and Shyam, 2024).

Obesity is caused by energy imbalance when energy intake is more than energy expenditure, leading to change in body composition and body weight gain (Bray *et al.,* 2016). The *C. forskohlii* plant has been indicated to promote lipolysis in order to attenuate lipid accumulation. In addition, The *C. forskohlii* plant was indicated to increase energy expenditure through promote fatty acid β-oxidation. Furthermore, *C. forskohlii* plant supplementation in combinations of other medicinal plant is decreasing the Firmicutes/Bacteroidetes to attenuate obesity (Tung *et al.,* 2021).

Forskolin is an active compound extracted from the *Coleus forskohlii* plant (Amezcua *et al.,* 2022; Roshni and Rekha 2024). It is a versatile compound with a wide range of potential functions including loss of body weight, increase muscle mass, relieve asthma, improve diabetes, improve cardiovascular health and increase blood flow to the brain and protect neurons from damage (Abbasi *et al.,* 2023).

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Forskolin is available in a variety of forms, including extracts, powders and capsules. The forskolin recommended dosage is depending on the form of the supplement and the body condition. Generally, forskolin is considered safe for most people when taken in a recommended dose.

Forskolin works by activating an enzyme called adenylate cyclase, which increases the level of cyclic AMP (cAMP). cAMP plays pivotal roles in many cellular processes, including cell growth, metabolism and inflammation (Shaikh and Finlayson, 2012; Rakhmanova *et al.,* 2023). cAMP is a second messenger used intracellular for signal induction and involved in lipid, sugar and glycogen metabolism regulation (Alasbahi and Melzig, 2012). The potential benefits of forskolin is to promote weight loss by increasing lipolysis and thermogenesis. Forskolin supplementation

led to significant reductions in body fat and body weight gain in overweight and obese adults (Godard *et al.,* 2005; Bonetti *et al.,* 2022). Therefore, the aims of this study were to investigate the changes in final body weight gain, liver weight: to body weight ratio, rectal temperature and blood glucose levels of control and *Coleus forskolin* groups. In addition, the changes in serum biochemistry (total protein, albumin, glucose and blood urea nitrogen) is also investigated.

MATERIALS AND METHODS

The experimental procedure was approved by the ethical committee [Ref. No. KFU-REC-2024-APR-EA000146] of King Faisal University. The *Coleus forskolin* leaves were purchased from farm located in Gazan area of Saudi Arabia. The experimental procedures were carried out in the experimental animal lab of Agriculture and Food Sciences College of KFU University.

Site of study and animal management

The study was carried out during the period from April to June 2024 of animal and fish department animal lab. Thirty six albino mice of growing (body weight; 9.92±0.45 g), adult males (body weight; 33.97±1.2 g) and females (body weight; 31.76±0.70 g) were used for the experiment (Fig 1). Mice were kept in groups of sex animals in transparent cages (40×24×18 cm) of control and the *C. forskolin* groups. Mice were fed commercial pellet basal diet (Arasco, KSA), which composed of 2.9% fat, 3.2% fiber, 22.0% protein, 1% mixture of vitamins and minerals and 3300 kcal/kg energy. The ground basal diet was mixed with powder of *C. forskolin* leaves (1.50%) and pelleted. The chemical composition of *C. forskolin* leaves is indicated in Fig 2. Animals had free access to water and diets. Mice were kept controlled under 12 h dark and 12 h light cycle starting at 8 a.m. The temperature (°C) and relative humidity (%) during the experiment were controlled to 26.0±2.60°C and 53.0±8.0%, respectively. The *C. forskolin* feeding lasts for four weeks.

Body and liver weight

Body weights of growing and males and females were recorded before and after four weeks of feeding upon 12 h fasting. Liver weights (g) were recorded after cervical dislocation of animals.

Rectal temperature and blood glucose

Rectal temperatures and blood glucose values were monitored at starting and end of experiment. Body temperatures were recorded using clinical thermometer (Citizen). Blood glucose values were recorded using blood glucose meter (Contour TS 4052 Basel, Switzerland) (Mohammed, 2018). The tail vein was punctured and the drop of blood put on strips for measuring blood values.

Blood sample collection and analysis

Blood samples were collected from the orbital sinus (Hoff 2000) at the end of experiment from mice of control and the *C. forskolin* groups. The obtained blood samples were analyzed for chemistry analyzer (Skyla VB1). The readable serum parameters include total proteins, liver enzymes, blood urea and creatinine and iron values.

Statistical analysis

Body and liver weight, rectal temperature, serum biochemistry values of were statistically analyzed using

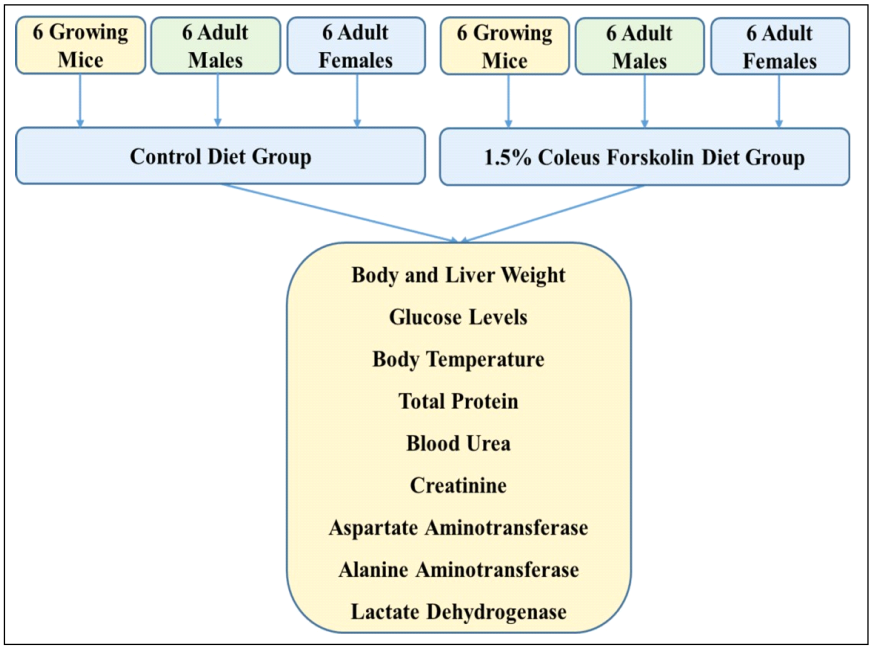

Fig 1: Experimental design of *C. forskolin* influences on body and liver weight, body temperature and serum profiles.

General Linear Model (G.L.M) procedure of S.A.S (S.A.S, 2000) according to the following model:

$$Yij = \mu+Ti+eij$$

Where:
μ = Mean.
Ti = Effect of *C. forskolin* (1.50%).
eij = Standard error.

Duncan's multiple range test (1955) was used to compare between means of the control and treated groups.

RESULTS AND DISCUSSION

Body and liver weight change over dietary *Coleus forskolin* supplementation (1.5%) in growing, adult male and adult female mice is presented in Table (1). The significant body weight loss of adult male and female mice was found in *C. forskolin* group compared to control one versus significant body weight gain in growing mice.

In addition, the rectal temperature values of control and *C. forskolin* groups are presented in Table (2). The significant hyperthermia in adult male and female mice was found in *C. forskolin* group compared to control one.

Glucose concentration changes over dietary *Coleus forskolin* supplementation (1.5%) in growing, adult male and adult female mice is presented in Table (3). The hypoglycemia in growing (P=0.001), adult males (P=0.06) and adult females (P=0.07) was recorded in *C. forskolin* group compared to control ones.

The biochemical serum parameters of control and *C. forskolin* groups are presented in Table (4). Generally, the data indicated inconsistency due to *C. forskolin* supplementation to growing mice, adult male and female mice. The inconsistency of results was observed in total protein, blood urea, creatinine, aspartate and alanine transferases and Lactate dehydrogenase values.

Results of the current study are presented in Table (1-4) indicating the effects of dietary *C. forskolin* leaves (1.5%). Dietary *C. forskolin* and its extract, forskolin (Amezcua *et al.*, 2022; Roshni and Rekha, 2024), were used for a wide range of potential functions including body weight loss, improve

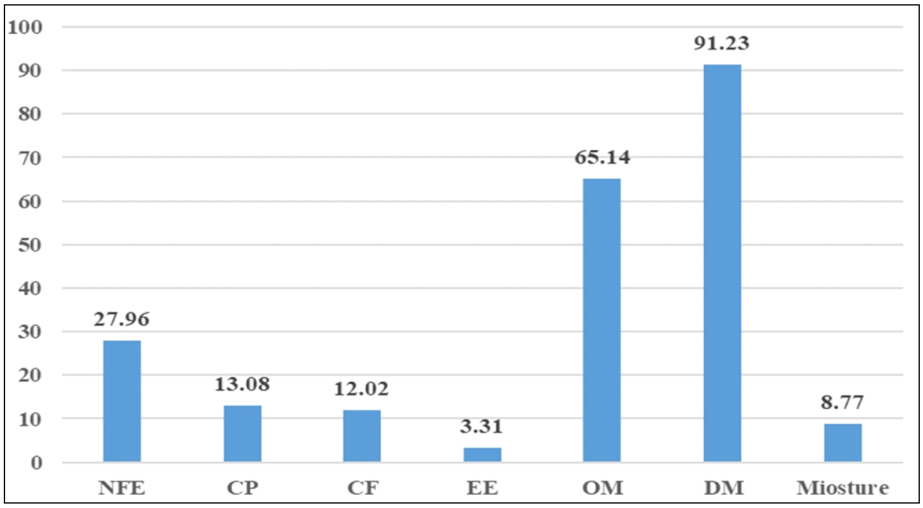

Fig 2: Chemical composition of dried *C. forskolin* leaves.

Table 1: Body and liver weight changes over dietary *Coleus forskolin* supplementation (1.5%) in growing, adult male and adult female mice.

Parameters	Control	*C. forskolin*	SE	P value
No. growing mice	6	6		
Initial body weight, g	9.92	9.92	0.45	0.97
Final body weight, g	16.03	16.4	1.41	0.05
Liver weight/body weight, %	NR	NR	NR	NR
No. adult male mice	6	6		
Initial body weight, g	34.06	33.88	1.28	0.40
Final body weight, g	42.46	40.38	0.95	0.001
Liver weight/body weight, %	6.83	6.52	0.32	0.05
No. adult female mice	6	6		
Initial body weight, g	31.63	31.9	0.75	0.86
Final body weight, g	39.10	37.96	1.40	0.001
Liver weight/body weight, %	6.44	6.49	0.44	0.15

NR: Not recorded; SE standard error.

diabetes and cardiovascular health, increase muscle mass and blood flow to the brain (Abbasi *et al.,* 2023). Generally, forskolin is considered safe for most people when taken in a recommended dose. The *C. forskolin* leaves (1.5%) of the current study were chosen as spice to food or drinks. Wang *et al.* (2009) and Kanne *et al.* (2015) explored the chemical constituents of *Coleus forskohlii*. Twelve compounds were isolated and identified including forskolin and rosmarinic acid. It was found through HPLC to measure the polyphenol content of aqueous leaf extracts of *C. forskohlii* that rosmarinic acid had the highest concentration (1.25 mg/g) compared to other polyphenols (Kundur and Shyam, 2024).

In our study, the *C. forskolin* dose was explored in growing mice, adult male and female mice. Surprisingly, the increase of body weight and decrease of glucose level of growing mice were more pronounced (p= 0.05) versus body weight loss of adult male and female mice (p= 0.001). This could be attributed to forskolin, which has been indicated to increase muscle mass (Abbasi *et al.,* 2023). Besides, forskolin works by activating adenylate cyclase, increases the level of cAMP, which in turn plays pivotal roles in many cellular processes, including cell growth and metabolism (Shaikh and Finlayson, 2012; Rakhmanova *et al.*, 2023). Furthermore, the significant body weight loss of adult male and female due to *C. forskolin* supplementation might be due to lipolysis and beta-oxidation (Zhang *et al.,* 2019).

In addition, the decrease of liver weight to body weight ratio were more pronounced in adult male of *C. forskolin* group might be due to increasing lipolysis. It has been found that the oral doses of 0.5 and 1.5/ mg/kg forskolin reduced fat in the liver (Zhang *et al.,* 2019). Furthermore, the increase of rectal temperature of *C. forskolin* group compared to control group is owing to forskolin effect on thermogenesis (Abbasi *et al.,* 2023).

The blood circulation and its profiles including serum components represents one of the most critical aspects of body health and physiology. Blood glucose values were decreased in growing (P=0.001), adult male (P=0.06) and adult female mice (P=0.07) of *C. forskolin* group might be due to forskolin effect as indicated in several studies (Abbasi *et al.,* 2023; Skelin *et al.,* 2023). The effects of dietary *C. forskolin* on serum metabolites are inconsistent among growing mice, adult males and female mice, which could be attributed to physiological condition and gender of mice (Mohammed, 2018).

Finally, the dietary *C. forskolin* is a supplement given to enhance the medicinal and nutritional status. It may contain one or more ingredients such as amino acids, metabolites, vitamins, minerals, herbs, or extracts. Dietary supplements are not suggested alone for treatment of a disease, but they should act synergistically with other treatments to facilitate healing or recovery. Though dietary ingredients may show certain effects in preclinical and clinical settings, the evidence may not be clinically significant in clinical trials (Gregg, 2005; Walter *et al.,* 2009; Batsis *et al.,* 2021). Thus, clinical studies and meta-analyses should be performed to prove the effectiveness of a dietary supplement. Moreover, different factors must be considered in selecting dietary supplements, among

Table 2: Rectal temperature changes over dietary *Coleus forskolin* supplementation (1.5%) in adult male and female mice.

Parameters	Control	*C. Forskolin*	SE	P value
Adult male mice				
Initial rectal temperature, °C	36.89	36.71	0.15	0.10
Final rectal temperature, °C	36.31	37.37	0.17	0.001
Adult female mice				
Initial rectal temperature, °C	37.07	37.01	0.16	0.56
Final rectal temperature, °C	36.83	36.98	0.14	0.001

SE standard error.

Table 3: Glucose concentration changes over dietary *Coleus forskolin* supplementation (1.5%) in growing, adult male and adult female mice.

Parameters	Control	*C. forskolin*	SE	P value
Growing mice				
Initial glucose, mg/dl	106.85	107.66	2.97	0.15
Final glucose, mg/dl	136.80	121.20	3.34	0.001
Adult male mice				
Initial glucose, mg/dl	108.66	108.83	3.85	0.80
Final glucose, mg/dl	118.66	115.0	3.60	0.06
Adult female mice				
Initial glucose, mg/dl	113.50	112.8	2.13	0.56
Final glucose, mg/dl	114.66	111.25	4.44	0.07

SE standard error.

Table 4: Plasma metabolites changes over dietary *Coleus forskolin* supplementation (1.5%) in growing, adult male and adult female mice.

Parameters	Control	*C. forskolin*	SE	P value
Growing mice				
Total protein, g/dl	5.4	5.0	0.28	0.001
Urea, mg/dl	25.0	23.0	1.13	0.06
Creatinine, mg/dl	0.4	0.7	0.048	0.001
Aspartate aminotransferase, U/l	173.0	185.0	16.19	0.07
Alanine aminotransferase, U/l	204.0	231.0	14.50	0.10
Lactate dehydrogenase, U/l	793.0	801.0	63.80	0.50
Adult males				
Total protein, g/dl	4.1	4.9	0.25	0.001
Urea, mg/dl	19.0	24.0	1.10	0.001
Creatinine, mg/dl	0.6	0.5	0.05	0.001
Aspartate aminotransferase, U/l	234	137	15.10	0.001
Alanine aminotransferase, U/l	251	182	12.50	0.001
Lactate dehydrogenase, U/l	826	801	43.60	0.70
Adult females				
Total protein, g/dl	4.1	3.9	0.22	0.001
Urea, mg/dl	20	26	1.09	0.001
Creatinine, mg/dl	0.5	0.7	0.049	0.001
Aspartate aminotransferase, U/l	130	204	13.10	0.001
Alanine aminotransferase, U/l	152	219	13.55	0.001
Lactate dehydrogenase, U/l	519	816	53.60	0.001

SE-Standard error.

which purity of the supplement, the patient's overall lifestyle (such as dietary habits and exercise), other health-associated conditions of the patient (such as concomitant diseases and nutritional status), accurate dosage, food-drug interactions, absorption profiles and potential side effects are the most relevant (Ríos-Hoyo and Gutiérrez-Salmeán, 2016).

CONCLUSION

The dietary *C. forskolin* leaves supplementation resulted in significant increase of body weight in growing mice versus body weight loss in adult female and male mice. The occurrence of hyperthermia and hypoglycemia was dependent on body condition and gender of mice upon *C. forskolin* leaves supplementation. Furthermore, green *Coleus forskolin* leaves might be used as feed additive since no negative effects was detected neither on liver function or serum profiles. Further studies are required for exploring *C. forskolin* effects through the level of supplementation and the physiological body conditions during peripartum period.

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Conflict of interest

There is no conflict of interest for authors to declare.

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