Fertility control impact of the aerial parts Ferula tingitana L. via alteration of hypothalamic-pituitary-gonadal axis responses of female Wistar rats

Abeer M. El Sayed 1*, Waleed El ghwaji1,2, Zeinab M. Yousef 3, Kadriya S. El-Deeb 1, Aly M. El Sayed 1

1Department of Pharmacognosy, Faculty of Pharmacy, Cairo University, Kasr El Aini, Egypt
2Department of Pharmacognosy, Faculty of Pharmacy, ElMergib University, Libya
3Department of Biochemistry, National Organization for Drug Control and Research, Giza, Egypt.

ABSTRACT

Ferula tingitana L. has been reported for abortive and/or menstruation inducing properties. However, its contraceptive effect has never been deliberately evaluated. Furthermore, no inclusive chemical profiling of its extract was recorded. Many Ferula species were known for their effects on the oestrogenic rhythm. During our drug discovery from natural sources F. tingitana L. growing in Libya was selected for evaluation of its contraceptive effect. To evaluate the hormonal effects and bioactive molecules of F. tingitana ethanol extract of aerial parts (EtOH) using in vivo experimental model. Adult female albino rats were divided equally into 4 groups (n=6). One group received distilled water for 14days, 2nd, 3rd and 4th groups received orally the tested extract at a daily dose of 100, 200 and 300 mg kg⁻¹ b.wt. for 14 days, respectively. The administration lasted for 14 days (2 weeks) at 9 A.M. Rats body and uterus weight were measured. They fasted overnight and then anaesthetized through a diethylether exposure and blood samples were collected through the ocular puncture. Blood was centrifuged to obtain clear sera for hormonal assay. The serum was subjected by ELISA method for assessment of follicle stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E2) and progesterone (P₄) levels. Biochemical estimations of total cholesterol (TC), triglycerlides (TG) and glucose (Glu) level were measured. GC/MS of the lipoidal profile along with HPLC analysis of the phenolic contents were carried out. EtOH and its successive soluble fractions were subjected for chromatographic analysis. The results displayed significant decrease in levels of FSH, LH, E₂ and P₄ of adult female Wistar rats. Significant decline in biochemical serum level of TC, TG and Glu were observed. Sesquiterpene daucol, linolenic acid, caffeic acid and hesperidin were the main identified phytoconstituents. CC of EtOH afforded 5 compounds were identified as β-sitosterol 1, collaridin 2, scopoletin 3, caffeic acid 4, 1-(3,4-dihydroxycinnamoyl) cyclopentane-2`,3`-diol 5. It was concluded that sesquiterpene coumarins as the significant phytoconstituents of EtOH may revealing adverse effect on the menstruation, ovulation of follicles and consequently may impair fertility. EtOH evidenced a hypoglycemic and hypocholesterolemic effects.

Keywords: Contraceptive, Ferula tingitana L., hypoglycemic, sesquiterpene coumarins.

Abbreviations: b.wt = body weight, EtOH = Ethanol extract, FSH= follicle stimulating hormone, LH = luteinizing hormone, E₂ = estradiol, P₄ = progesterone, TC=total cholesterol, TG = triglycerlides, Glu = glucose, GC/MS= gas chromatography/mass spectroscopy, HPLC=High performance liquid chromatography, CC=Column chromatography. ELISA= Enzyme Linked Immunoassay, SFA= Saturated fatty acids, USFA= Unsaturated fatty acids, USM= Unsaponifiable matter, SM=Saponifiable matter, FAME= fatty acid methyl esters, PE=petroleum ether extract

*Corresponding author: Abeer M. El Sayed
abeer.ali@pharma.cu.edu.eg
Received on 8/3/2021 and Accepted for Publication on 27/8/2021.
1. INTRODUCTION

Complications related to overpopulation comprise the enlarged demand for resources such as clean water and food, starvation and malnutrition, consumption of natural resources faster than the rate of regeneration, and deterioration in living conditions (1). Slowing population growth through lower fertility produces a demographic dividend, whereby the proportion of persons of working age increases with respect to that of children and the elderly. (1,2) Lowering fertility facilitates the achievement of key development goals. Countries with lower fertility and therefore slower population growth spend substantially more in the health and education of each child than those with higher fertility.(3)

The genus *Ferula* (Apiaceae) comprises about 150 species of flowering plants. Many of the biological features of this genus includes cytotoxic, antibacterial, antiviral, P-glycoprotein (P-gp) inhibitor, antiinflammatory, antileishmanial, antioxidant and others have been attributed to the sesquiterpenes-coumarins present. (4) In addition to saponins, essential oils and triterpenes were major constituents. (4, 5) Contraceptive carotene sesquiterpenes of *F. jaeschkeana* Vatke. were isolated and evaluated on the histological and biochemical elements of the uterus of ovarictomized rats. (6) The hexane extract of *F. jaeschkeana* was studied by Prakash et al (7) for its effects on the oestrogenic rhythm following a single administration to immature rats.

*Ferula tingitana* L. is a tall perennial herb and grows in scrubland and rocky areas. It is mainly expanded across Mediterranean coast in Spain, Morocco, Lebanon, Israel, Palestine, Cyprus and Turkey. It is reported for it is known for its abortive and/or menstruation induced properties.(8) Miski et al. (9) isolated sesquiterpene ester, tingitanol, from *F. tingitana* L., as well as, the petroleum ether extract of the roots of *F. tingitana* yielded daucane esters. (10) The volatile oil collected from plant growing in Libya evidenced cytotoxic, antifungal, and mild antibacterial effects. (11) Reviewing the current literature revealed that no experimental study was adapted to prove the folkloric use of the plant under investigation as contraceptive drug. So, the aim of this work is to explore bio-active compounds from the aerial parts of *F. tingitana* L. since the scientific validation of traditionally used plant in treatment is highly demanded. Also, to contribute new knowledge to the currently existing known chemical/or biological data about *F. tingitana* L. is growing in Libya.

2. Material and methods

2.1. Plant material

Aerial parts of *Ferula tingitana* L. were collected in March 2014 from the West Mountain, Mislata, Libya https://goo.gl/maps/uzhPwzwWGGwEGAiFA. Plant identity was kindly authenticated by Dr. Reem Samir Hamdi, professor of plant taxonomy, Botany Department, Faculty of Science Cairo University, Egypt. Drying and grinding of plant material were done in Medicinal, Aromatic and poisonous plant Experimental station, Cairo University. Voucher samples (1-5-2014.) are kept at the herbarium of the Pharmacognosy Department, Faculty of Pharmacy Cairo University https://goo.gl/maps/Y9Ug8RR7WWb7CCHe6. EtOH of the aerial parts of *F. tingitana* was dissolved in 1% Tween 80 to prepare solution of concentration of 150 and 300 mg/ml and used for pharmacological studies.

2.2. Extraction and fractionation

The air dried powdered aerial parts of *F. tingitana* L.(1.5kg) was extracted with 2.5L ethanol (90%) by cold maceration till exhaustion. The collected EtOH were evaporated to yield 195g of dark green residue. EtOH extract (100g) was suspended in 400 ml of distilled water and partitioned successively. The solvent free extractives were weighed and amounted to 30, 15,7 and 25 g for petroleum ether, methylene chloride, ethyl acetate and n-butanol, respectively. In addition, there was 23g of insoluble matter.

2.3. Drugs and biochemical kits

Aluminium chloride, Sodium carbonate, Gallic acid and Rutin were obtained from Sigma Aldrich (St. Louis,
MO, USA). All the chemicals used, including the solvents, were of analytical grade. Biodiagnostic kits: A Glucose kit (Bio-Merieux Co, France) was used. Assay kits for progesterone, estradiol, follicle stimulating hormone and luteinizing hormone were supplied by Sigma-Aldrich Chemicals, Pomona/Kempton Park 1619, and Johannesburg, South Africa. Assay kits for glucose, cholesterol and triglycerides were procured from Randox Laboratories Ltd, Co-Atrim, United Kingdom. All other reagents used were of analytical grade and were prepared using glass-distilled water.

2.4. Phytochemical studies

Gas chromatograph/Mass spectrometric (GC/MS) apparatus for unsaponifiable matter analysis. Gas liquid chromatograph, GC Ultra system (Thermo Fisher scientific Co., USA), kept at the central laboratory. Faculty of Agriculture, Cairo University (Giza, Egypt) for analysis of fatty acid. HPLC system (GBC-LC) high performance chromatograph equipped with LC 1150 quaternary gradient pump and LC1210 k program mabledaw wavelength UV detector (GBC scientific equipment, Melbourne Australia) in the food technology research institute, Faculty of Agriculture, Cairo University (Giza, Egypt) for analysis of phenolics. UV-Visible Spectrophotometer, Shimadzu UV-1650 PC was used for recording UV spectra and measuring the absorbance in UV range. InfraRed spectrophotometer, Shimadzu IR-435, PU-9712 was used for recording IR spectra using KBr discs. EI-MS was recorded on a Varian Mat 711 or SSQ 7000 (Finnigan mat) system. The instrument was equipped with a DB-5 column (30m × 0.25 mm i.d., 0.25 μm film thickness); J&W Scientific, USA. Operating conditions: Injection volume, 1μl of CH2Cl2 solution of tested samples; oven temperature programming: initial temperature, 40°C (isothermal for 3 min), then increased (4°C/min) to 160°C, followed by further increased to final temperature 280°C (10°C/min); injection temperature: 220°C carrier gas: helium at a flow rate of 1ml/min; mass spectrometer, electronic ionization(EI)mode; ion source, 70eV; mass range:40- 500 amu. Identification of the constituents was achieved by library search on a Wiley 275 L GC-MS data base, observed mass fragmentation patterns to those of the available references as well as of published data. A series of authentic n-alkanes was subjected to GC under the same experimental conditions. The individual components were determined by computerized peak area measurement. Compounds of the USM and percentage composition are compiled (Table 1). The FAME sample was analyzed using GLC Trace GC Ultra system equipped with FID detector. Analysis was performed using a Thermo TR FAME column (70% Cyanopropyl Polysilphenylene Siloxane) (30mx 0.25mmx 0.25μm film thickness); injector temperature 200°C, using N2 as carrier gas and adopting a temperature programming as initial temperature, 140°C, increased to 200°C by the rate of 5°C/min, then kept isothermal for 3min. Flow rate 30ml/min. with N2 as carrier gas. Aliquots, 2 μL each, of 2% chloroformic solutions of the analyzed FAME and reference fatty acid methyl esters were analyzed under the same extract (PE) 1.0 g. The solvent-free residue (0.30g), representing the USM, was saved for further GC/MS analysis. The aqueous alkaline solution, left after separation of the USM, was acidified with dilute hydrochloric acid (5N) to liberate the free fatty acids (FA), yielding a 0.60g residue representing the free FA. The FA mixture as well as the standard fatty acids was, saved for GLC analysis.

The USM was subjected to gas chromatography/mass spectrometry (GC/MS) analysis which performed using a Thermo Trace GC 2000 (Thermo Quest, TX, USA)/MS Finnigan mat SSQ7000 system. The instrument was equipped with a DB-5 column (30m × 0.25 mm i.d., 0.25 μm film thickness); J&W Scientific, USA. Operating conditions: Injection volume, 1μl of CH2Cl2 solution of tested samples; oven temperature programming: initial temperature, 40°C (isothermal for 3 min), then increased (4°C/min) to 160°C, followed by further increased to final temperature 280°C (10°C/min); injection temperature: 220°C carrier gas: helium at a flow rate of 1ml/min; mass spectrometer, electronic ionization(EI)mode; ion source, 70eV; mass range:40- 500 amu. Identification of the constituents was achieved by library search on a Wiley 275 L GC-MS data base, observed mass fragmentation patterns to those of the available references as well as of published data. A series of authentic n-alkanes was subjected to GC under the same experimental conditions. The individual components were determined by computerized peak area measurement. Compounds of the USM and percentage composition are compiled (Table 1). The FAME sample was analyzed using GLC Trace GC Ultra system equipped with FID detector. Analysis was performed using a Thermo TR-FAME column (70% Cyanopropyl Polysilphenylene Siloxane) (30mx 0.25mmx 0.25μm film thickness); injector temperature 200°C, using N2 as carrier gas and adopting a temperature programming as initial temperature, 140°C, increased to 200°C by the rate of 5°C/min, then kept isothermal for 3min. Flow rate 30ml/min. with N2 as carrier gas. Aliquots, 2 μL each, of 2% chloroformic solutions of the analyzed FAME and reference fatty acid methyl esters were analyzed under the same
conditions. Identification was based on comparing the retention time of their peaks with those of the available reference standards. The amount of each component was calculated by peak area measurement using a computing integrator.

**Spectrophotometric determination of phenolic and flavonoid contents**

The total phenolic and flavonoid contents were determined in the aerial parts of *F. tingitana* according to published spectrophotometric procedures.\(^{(13, 14)}\) The total phenolic content was expressed as Gallic acid equivalents (mg GAE/100mg extract) and deduced from the pre-established calibration curve. Triplicate experiments were carried out for each sample. Colorimetric method was adopted, based on measuring the intensity of the color developed when flavonoids are complexed with aluminum chloride method.\(^{(13, 15)}\) The total flavonoid content was calculated from a calibration curve, and the result was expressed as mg rutin equivalent per 100 mg extract. Experiments were carried out in triplicates, and average absorbance values recorded.

**2.6. HPLC analysis of polyphenols contents**

HPLC Agilent (series 1100) equipped with autosampling injector, solvent degasser, ultraviolet (UV) detector set at (280 nm for phenolics determination and 330 nm for flavonoids determination) and quaternary pump. The column temperature was maintained at 35°C temperature for each. The column used for separation was zorbax ODS 5μm (4.5×250mm), Gradient separation was carried out using methanol and acetonitrile (2:1) as a mobile phase at flow rate of 1 ml/min. Authentic phenolics and flavonoids were dissolved in mobile phase and injected into HPLC. The retention time and peak area were used to calculate the phenolic and flavonoids concentrations by the data analysis of Hewllet packared software \(^{(16, 17)}\). The simultaneous separation and quantization of flavonoids, catechins and phenolic acids were performed on an analytical HPLC system consisting of GBC-LC high performance chromatograph equipped with a UV detector set at two different wavelengths 280 and 330 nm. Analysis was achieved on a Hypersil BDS C18 column (250 mm× 4.6 mm, 5μm particle size).

**2.7. Chromatographic analysis of different extractives of *F. tingitana* L.**

The petroleum ether fraction (10g) was fractionated on a silica gel column VLC (15x20cm). Gradient elution was carried out. Fraction (B): 3g eluted with 30-40% CH₂Cl₂ in n-Hexane) was rechromatographed, to yield pure compound 1 (13 mg, \(R_f= 0.37\), in S₂) as white powder. Fraction (C): 2.7g eluted with 50-90% EtOAc in CH₂Cl₂) were similarly rechromatographed on a silica gel (60g) column (60×2cm)using n-hexane: EtOAc (7:3 v/v) as eluent, fractions (10 mL, each) were collected. For further purification, this residue was applied to a silica gel (20g) column (50×1.5cm) and eluted with CH₂Cl₂:MeOH (9:1 v/v), yielding white needle crystals of compound 2 (20 mg, \(R_f= 0.67\), in S₃).

Seven grams of methylene-chloride soluble fraction was fractionated on silica columns VLC (15x20cm). Gradient elution was carried out. Fraction II (3g, eluted with methylene chloride:methanol(8:2 v/v), were rechromatographed; sub-fractions IIₐ rechromatographed on silica gel column solvent system using CH₂Cl₂-EtOAc (1:1) to yield pure compound 3 (13 mg, \(R_f= 0.65\) in S₃) as yellow amorphous powder. Sub-fractions IIₐ were eluted by CH₂Cl₂-MeOH (9:1), showed three spots after spraying with \(p\)-anisaldehyde, were rechromatographed on silica gel using by gradient elution with EtOAc-CH₂OH (9:1) solvent system to give two major spot with \(R_f\) value 0.7 in S₄, the fractions were pooled and evaporated to yield two compounds 4 (22 mg).

Ethyl acetate fraction (4g) was chromatographed on diaion column (3.5x50 cm), packed with diaion (50 g). Gradient elution was carried out using H₂O, MeOH and Acetone (increasing percentage 10 – 25%). Similar fractions were pooled together to yield three main fractions coded from D1 to D3. According to the results of thin layer chromatographic investigations the most promising fractions (D2 and D3) were collected and subjected to
further chromatographic purifications using silica gel columns to afford one compound 5 (25 mg, \( R_f = 0.65 \) in S₃) as yellow amorphous powder.

**Animals**

Twenty-four adult female albino rats (Wistar strain, 150-200 g) were used for assessment of the hormonal and protective activity on glucose, total cholesterol and triglyceride levels in rats. Animals were obtained from the National Organization for Drug Control and Research (NODCAR), Cairo, Egypt. Animals were housed in an air-conditioned atmosphere, at a controlled temperature of 24 ± 1°C with alternating 12 h light and dark cycles and kept on a standard pellet diet and water *ad libitum*. The animals were acclimatized for one week before experimentation. They were screened and observed to exhibit regular estrous cycle. The study protocol complies with the Guide for the Care and Use of Laboratory Animals (NIH Publication No. 85-23, revised 1996) and was approved by the Ethics Committee for Animal Experimentation, Faculty of Pharmacy Cairo University, Egypt.

**2.8. Experimental protocols**

The selected animals were randomly divided equally into 4 treatment groups containing 6 six rat each (\( n=6 \)). Group I: Animals were given distilled water for 14 days served as control group. Group II, III and IV: Animals received orally the tested extract at a daily dose of 100, 200 and 300 mg kg⁻¹ body weight /day for 14 days respectively as nearly 1/20, 1/10 and 1/6 of the LD₅₀. The administration lasted for 14 days (2 weeks) at 9 AM. EtOH was prepared at fixed dose of 2000 mg/kg, p.o for 14 days according to Organization for economic cooperation and development OECD guideline NO 423. The administration was conducted by analysis of variance (ANOVA) followed by Tukey's test using the Statistics software IBM-SPSS, (Armonk, NY, U.S.A.) version 20. The significance level was set at \( P < 0.05 \).

**3. Results**

**3.1. GC/MS analysis of the unsaponifiable matter (USM)**

GC/MS analysis of the USM is illustrated in Table 1 which revealed that fenchyl acetate 18.69% was the major hydrocarbon detected. Whereas stigmasterol 1.53% and phytol 35.25% were the major sterol and diterpenes detected, respectively. Phytol was chiefly reported in genus *Ferula*. (23) Sesquiterpenes components were up to 24.22% of which daucol 16.79% was the major unique. Terpenoid constituents may justify the anti-inflammatory effect previously reported. (24)
3.2. GLC analysis of the fatty acid methyl esters (FAME)

GLC analysis of FAME (Table 2) revealed that the USFA constituted 51.45%. α-Linolenic acid (ALA) 36.75% was the major USFA. Arachidonic acid 11.19% is a fatty acid most found in peanut oil that is responsible for muscle tissue inflammation. (25) Saturated fatty acids (SFA) constituted 22.26%, among which palmitic acid 8.56% was the major one. USFA constituted more than double the percentage of the SFA.

3.3. Determination of total phenolic and total flavonoid contents

The average absorbance of ethanol extract were 0.437 and 0.265 corresponding to 19.63 and 61.86 mg gallic acid and rutin/g dry powdered aerial parts respectively. Polyphenolic/ or flavonoids are existing in significant amounts in F. tingitana L and further study is needed to explore their constituents. Total phenolic and flavonoid contents of Apiaceae species such as F. gummosa Boiss previously reported. (26)

3.4. HPLC analysis of polyphenolic compounds

HPLC analysis of the aerial parts of F. tingitana L. enabled the identification and quantification of 23 phenolic compounds among which: 13 phenolic acids, 10 flavonoids. The main detected phenolic acids were caffeic acid and gallic acid with concentrations 1192.08 and 344.49 ppm respectively. On the other hand, the major identified flavonoids were hesperidin and quercetin with respective concentrations 1156.3 and 87.75 ppm (Tables 3, 4).

3.5. Identification of the bioactive compounds

Five compounds were isolated from the aerial parts of F. tingitana L. and characterized through MS, IR, 1H, 13CNMR and 2DNMR data as well as by comparison to previously reported ones. Compound 1 is identified as β-sitosterol. (27) Based on the spectral data (Table 5) compound 2 could be identified as sesquiterpene coumarin, colladonin. (28, 10) The 1HNMR spectrum of compound 3 displayed signals characteristics of a 6,7-dioxxygenated coumarin (Table 5) therefore, identified as scopoletin. On the basis of the previous found and published data (29) compound 4 was identified as caffeic acid (Table 5). The presence of caffeic acid in F. tingitana may hint some free radicale quenching effect and/or cancer chemo preventive property. Comparison of the represented spectroscopic data of 5 (Table 5) with those reported in the literature (30) revealed that 5 is identified as 1-(3,4-dihydroxycinnamoyl)cyclopentane-2,3-diol.

3.6. In vivo assessed hormonal activity

3.6.1. Effect on body and reproductive organ weight (uterus)

Results depicted in Table 6 and Figure 3 revealed that administration of the tested extract 200, 300 mg kg⁻¹ was significantly decreased the body weight gain and reproductive organ (uterus) in dose depended on manner.

3.6.2. Effect on the levels of different serum hormones

Administration of EtOH of F. tingitana L. for 3 weeks was significantly decreased the serum levels of FSH, LH, E2 and P4 in dose depended on manner (Table7& Figure4). 3.6.3. Effect on the triglycerides, total cholesterol, and glucose level

As compared with the control group, only dose 300mgkg⁻¹ of ethanol extract of F. tingitana L. was able to decrease triglycerides and glucose level (Table 8 and Figure 3). Earlier investigators revealed that F. tingitana L. has a hypolipidemic effect marked by decline in the levels of triglyceride on the rats treated with ethanol extract of F. tingitana L.

4. Discussion

Growing human population through the world particularly in developing and underdeveloped countries has damaging effects on life supporting system on earth. Usually, plants have been used to treat different kinds of ailments. Ferula gummosa exhibits change in the body weight of diabetic rats. (31) The reduction in the levels of follicle stimulating hormone may hamper folliculogenesis and delay maturation of the follicle in the pre-ovulatory phase.(32) Prior investigators, Yusufoglu et al.,(33) have
confirmed the hypoglycemic effect of various *Ferula* species. Oral contraceptive gents have been used to reduce fertility rate, but their unusual side effects limit their use. (34) Plants have been used to treat different kinds of ailments including. The contraception ability of plants has been reported in several animal models. (35) Historically, plants have been a source of drugs, but no scientific experiments prove the importance of herbal medicine as antifertility agents. (36) The World Health Organization suggested that effective, locally available plants can be used as alternatives for drugs. (37) *Ferula assa-foetida* L. was proved a potential antifertility effect. (38) It is likely that the EtOH of *F. tingitana* might have exerted its effect on the anterior pituitary or the hypothalamus since the secretion of stimulating hormone is regulated by the gonadotropic releasing hormone secreted by the hypothalamus. The observed reduction in level of serum LH indicates the inhibitory effect of the extract on the release of LH which may trigger disruption of ovulation. (39) This may result in impairment of estrous cycle, hamper conception and normal reproduction in the females. Decrease in P₄ hormone level through 300mgkg⁻¹ of *F. tingitana* prevent thickening of myometrial lining also ovary can be not imbedded and so increase sensitivity to oxytocin. Decrease in E₂ level may hinder ovulation, preparation of the reproductive tract for zygote implantation and the subsequent maintenance of pregnancy state. (40) *Ferula Hermon* was previously reported to induce decrease in the serum hormonal level of LH and FSH. (41) *Ferula narthex* Bioss showed anti-fertility effect. (42) Anti-infertility effect previously reported to several *Ferula* species may be attributed to their sesquiterpenes coumarins contents. (43) Sesquiterpenoid compounds were detected as major constituents presented by daucal in *F. tingitana* L. Results observed in this study are comparable to the previously reported. (10) Daucane-type sesquiterpenes was isolated from the methanol extracts of the air-dried roots and stems of *F. kuhistanica*. (44) Likewise, aerial part of *F. tingitana* is rich in ALA as seed oil from Rosa mosqueta (*Rosa rubiginosa*), sachainchi (*Plukene tiavolubis*), canola, sunflower, and chia (*Salvia hispanica*) which may constitute an alternative that merits research. (45) Polyphenolic are existing in significant amounts in *F. tingitana* L. Total phenolic and flavonoid contents of Apiaceae species such as *F.gummosa* Boiss previously reported. (26) Reviewing the available literature, β-sitosterol and colladonin were previously isolated from *F. tingitana* L. To the best for our knowledge, this is the first report for the isolation of scopoletin, caffeic acid, and 1-(3,4-dihydroxycinnamoyl) cyclopentane-2,3-diol from the aerial part of *F. tingitana* L.

5. Conclusion
Ethanol extract of the aerial part of *F. tingitana* assure its use as a contraceptive agent through diminution of the hypothalamic-pituitary-gonadal axis hormones. An alteration on the hypothalamic-pituitary-gonadal axis responses presented on the female reproductive hormones of adult female *Wistar* rats were noticed as adverse effect on the menstruation, ovulation of follicles and consequently may impair fertility mediated through the synergistic effect of the secondary metabolites mainly, sesquiterpenes coumarins. Though, the more comprehensive fundamental mechanism deserved additional inquiry.

Declaration of competing interest
The authors declare that there is no conflict of interest.

Authors’ contribution
REFERENCES


(19) Uotila M, Ruoslahti E, Engvall E. Two-site sandwich enzyme immunoassay with monoclonal antibodies to

(20) King E J, Garner, R J. The Colorimetric Determination of Glucose. J clin pathol. 19471;(1);30–33. doi:10.1136/jcp.1.1.30


(40) AL-Shemary N N A, Mousa S A, Muslim Z Z. Histological and hormonal study about the effect of aqueous extract of ocimum gratissimum on female reproductive system in albino mice. J Pharmaceut Sci


Fertility control impact... Abeer M. El Sayed, et al.,


tأثير التحكم في الخصوبة بالأجزاء الهوائية لنبات الجريبوتا تتجيتيانا عن طريق تغيير استجابات محور الوطاء - الغدة النخامية - التنازلية لإفان فترات ويستار

عبير محمد على السيد۱، وأيد الجهوجي۲، زينب يوسف۳، قدرية شفيق الديب۴، على محمد السيد۵

۱قسم العقاقير، كلية الصيدلة، جامعة القاهرة، مصر.
۲قسم العقاقير، كلية الصيدلة، جامعة المرقب، ليبيا.
۳قسم الكيمياء الحيوية، الهيئة القومية للرقابة والبحوث الدوائية، الجزيرة، مصر.

ملخص

تم الإبلاغ عن F. tingitana L. لخصائصه المحيضية وأو السمية للحيض. ومع ذلك، فإن تأثيره في منع الحمل لم يتم تقييمه بشكل محدد. علامة على ذلك، تم تجربة النبات في اقتصاص الأشجار المنخفضة. نجا العديد من أنواع الكورول بتأثيرها. F. tingitana L. على إيقاف الدراسات في خلال 8 أسابيع من الساماتن الطبيعية، تم اختبار الحشيشة في مجموعة من الفئران. تأثير النبات والهجوميات بصفة عامة، تم تقليل انتاج الفئران البيضاء البالغة بنسبة 40% في المجموعات الخضراء والثالثة ورابعة. المستقبل الخضري عن طريق المجمد بجرعة يومية من 100 و300 مجم / كجم. - 24 -

الكلمات الدالة: موائع الحمل، F. tingitana L.