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ANTIFERTILITY EFFECTS OF THE PETROLEUM ETHER EXTRACT OF *PHYSALIS MINIMA* ON FEMALE ALBINO RATS

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ABSTRACT

Oral dosing of the *Physalis minima* L. (Solanaceae) petroleum ether extract to female albino rats altered the regular cyclicity. Rats treated with the extract exhibited variations in uterine and ovarian weights and caused significant histopathological changes in the histoarchitecture of ovary, oviduct and uterus. Extract administration showed inhibitory effects of a transient nature. This is the first report of histopathological observations on a female system after *Physalis* treatment.

INTRODUCTION

Since the Vedic era, mankind has been dependent on plant products for food and healthcare. Of the 250,000 higher plant species on Earth more than 80,000 have a medicinal use. Around 2,500 species have been thoroughly screened for pharmacological activity. During 1968–81, as many as 201 extracts from different parts of 36 plants were reported to possess contraceptive properties, and were tested for such activity (Garg et al., 1978; Garg, 1981). This area of study, dealing with an interesting and potentially useful group of phytoconstituents, needs further exploration, through a broad biological screening programme (Bhargava, 1986). WHO has been doing such screening for years in its study centres.

Keywords: *Physalis minima* L., Solanaceae, estrus cycle, female fertility, histoarchitecture, histopathology, ovary, oviduct.

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There are several reports on the medicinal aspects of *Physalis* species (Chopra et al., 1956; William et al., 1976; Dhawan et al., 1977) and phytochemical studies indicating the presence of steroid lactones, physalins and withanolides (Kawai et al., 1969; Matsuura & Kawai, 1969). Murugesa Mudhaliyar (1936), in his *Materia Medica* (Vegetable Section, Vol. I), reported *Physalis minima* L. as having both diuretic and aperient properties. Mohana et al. (1979) reported the abortifacient activity of Physalin-x isolated from *P. minima* in female albino rats. The effects of an aqueous extract of *Physalis alkekengi* L. fruit on estrus cycle, reproduction and uterine kinase BB isozyme in rats was demonstrated by Vessal et al. (1991). There is no work on the histopathological changes caused by the administration of *Physalis* on animal systems in general and fertility studies in particular. For this reason, we have studied the antifertility effects of the petroleum ether extract of the *Physalis minima* L. (Solanaceae) on female albino rats.

MATERIALS AND METHODS

Fresh leaves of *Physalis minima* L. (Solanaceae) were collected from the natural populations of South India and shade dried. Voucher specimens were deposited in the Botanical Survey of India, Southern Zone, Coimbatore (MH/160/161 – 160165). Vouchers were identified by Dr. Mahinda Martinez, Mexico. The aerial parts were powdered and then extracted in a Soxhlet apparatus by hot continuous process using petroleum ether for 24 h. The extract was concentrated under vacuum to produce a residue. The residue was dried in a desiccator at 50°C.

Female albino rats (weighing 200–250 g), were procured from Padapai, Tamil Nadu. The animals were

maintained in an air conditioned room and fed standard pellet diet (Hindustan Lever Ltd., Bombay) and water *ad libitum*. The animals were exposed to a photoperiod regimen of 14/10 h light and dark. The animals were divided into control and treatment groups each with 24 animals. The experimental group received an oral dosage of 1/8th of the LD₅₀ (LD₅₀ = 1 g/1 kg) for 8 consecutive days, while the control group received the same quantity of distilled water in the same manner. To define the stages of the estrus cycle, vaginal smears were prepared and examined from all animals between 7.30 to 10.30 h daily. The weights of the rats were recorded every four days. After the last treatment the rats were killed by a blow on the head and organs such as the ovary, oviduct and uterus, were dissected and their weights recorded. Then the organs were fixed in alcoholic Bouin's fluid for histopathological observations. Paraffin sections (5 μm thick) were taken and stained with haematoxylin and eosin. Photomicrographs were taken using Nikon photomicroscopy. Statistical analyses were carried out according to the methods of Gomez and Gomez (1976).

RESULTS AND DISCUSSION

Effects on Estrus Cycle

The stages of the estrus cycle of the control group receiving oral dosage of distilled water and those of the treatment group receiving the *Physalis* extract were studied. The control group showed a normal cycle of 4–5 days whereas the treatment group showed variations in 60% of the rats. An average of 4–6 days are needed to retain their normal cycle after the last day of treatment whereas a previous study on rats using *P. alkekengi* fruit extract by Vessal et al. (1991) showed 100% irregularities in the estrus cycle, which is reversible after 8 days. Various studies on estrus cycle using gossypol (Lin et al., 1995), an estrogen antagonist CN-55, 945-27 (Calantine et al., 1966) have showed only 65–75% variations in cyclicity. From the present study it is inferred that rats which stayed in diestrus were reported to be in a stage of complete uter-

ine rest as reported by Fox and Laird (1970), since the resting uterine stayed in the diestrus stage after treatment and retains its original cycle after withdrawal of the drug.

From the present study it is clear that the administration of the drug not only altered the cyclicity but also the total body weight, uterine weight and ovary weight (Table 1). The difference in total body weight between the control and treatment groups is not statistically significant. However, significant reduction in wet weight of the ovary was observed. Kalra and Prasad (1967) reported reduction in ovary weight on long term administration of clomiphene. The low uterine weights obtained in the present study indicated that this could be due either to a low level of estrogen as a result of suppression of pituitary gonadotrophins and or to its anti-estrogenic activity as stated earlier by Kalra and Prasad (1967).

Histopathological Studies

Oral administration of the petroleum ether extract of *Physalis minima* caused numerous histopathological changes in the histoarchitecture of the ovary, oviduct and uterus.

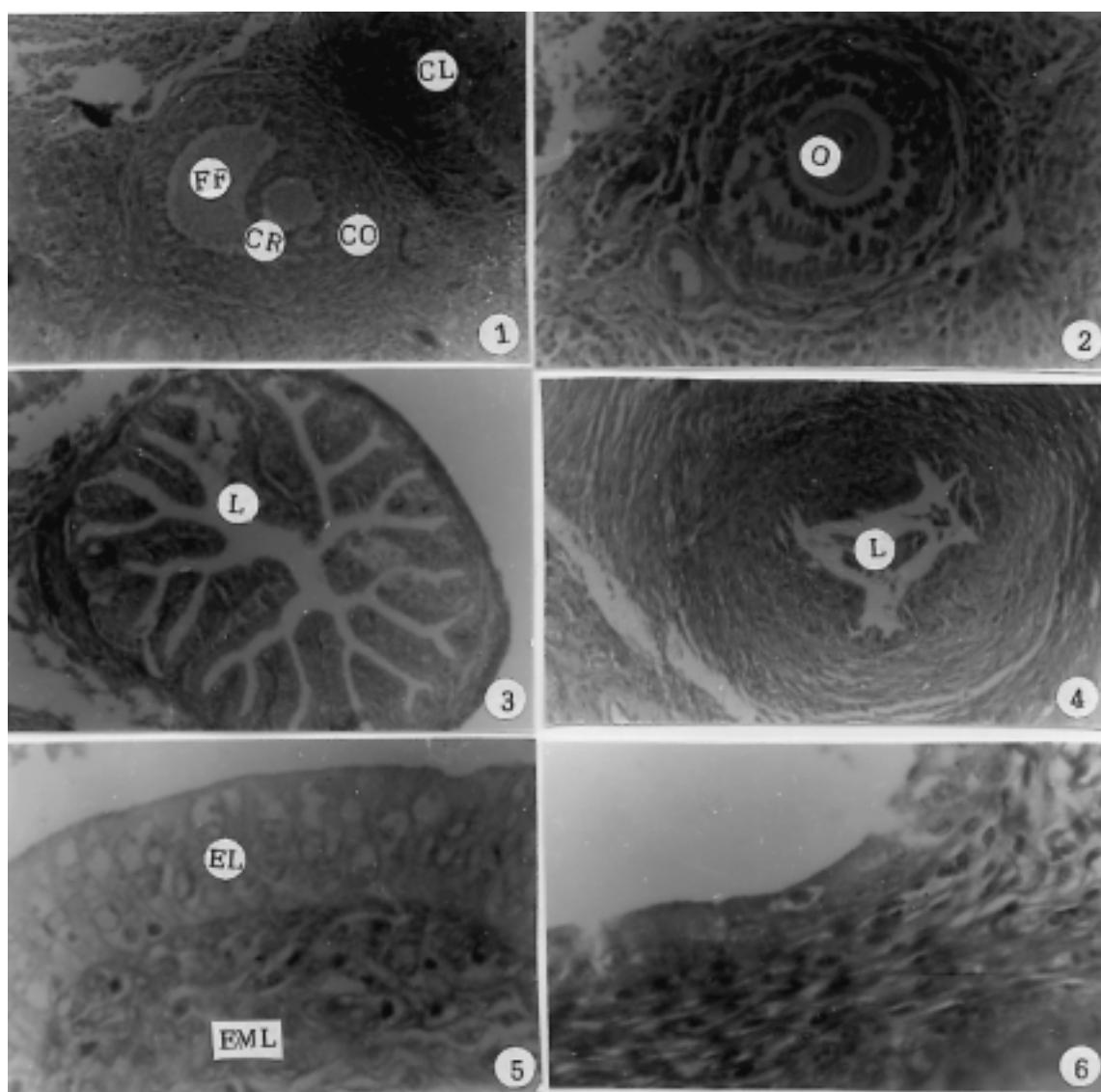
Ovary

Ovarian histopathological architecture showed significant alterations after treatment with the *Physalis minima* extract. The control ovary showed the presence of graafian follicles in all stages of development and functional corpora lutea. Interstitial tissue was normal. The matured graafian follicle was normal with oocyte surrounded by cumulus oophorus and corona radiata cells and the antrum was filled with follicular fluid (Fig. 1.1). The treated ovary showed atretic follicles and exhibited marked pycnosis of the granulosa cells. Corpora lutea were absent and the interstitium was entirely fibrocellular with poor vascularity. The graafian follicles showed hypertrophy, granulation and vacuolation. Stroma was fibrotic and nuclei were darkly stained. The cumulus oophorus and corona radiata cells degenerated, leading to the loss of nutrition to the oocyte (Fig. 1.2). Similar results were observed by Kalra and Prasad (1967) and

Table 1. Effects of *P. minima* extract on body, uterus and ovary weights.

Experiment	n	Body weight	Uterus weight	Ovary weight
Control	24	243.91 \pm 3.31	399.04 \pm 2.47	41.91 \pm 0.66
Treatment	24	240.40 \pm 3.20	384.75 \pm 3.24	33.79 \pm 0.61

Values are SEM \pm SE.



1. Matured graafian follicle with follicular fluid and functional ovum (100 \times).
 2. Degenerated follicle showing hypertrophy (100 \times).
 3. Oviduct of the control animal (200 \times).
 4. Oviduct of the treated animal (200 \times).
 5. Uteri of the control animal showing lumen and epithelial lining (850 \times).
 6. Uteri of the treated animal (850 \times).
- CL – Corpus Luteum, CO – Cumulus Oophorus, EML – Endometrial Layer, O – Ovum, FF – Follicular Fluid, CR – Corona Radiata, L – Lumen, EL – Epithelial Lining.

Mathur et al. (1994) in their studies using other chemicals and plant principles. From the present study it is evident that follicular development was inhibited by the drug and resulted in the absence of corpora lutea.

Oviduct and Uterus

The oviduct of the control showed a well developed external muscular layer with inner lining of columnar epithelial cells and lumen filled with secretions. The lumen was normal (Fig. 1.3). The treatment group

showed the epithelial lining reduced to low cuboidal cells with dark stain and narrow lumen (Fig. 1.4). The uteri of the control rats exhibited a well differentiated serosa, muscularis and endometrial layers and broad lumen filled with secretions. Many well developed glands were present in the endometrium (Fig. 1.5). The uteri of the treatment group showed many necrotic features, columnar epithelium showed reduction in height with intense staining. Stroma showed fibrotic changes. Endometrium was broad and the lumen was narrowed

(Fig. 1.6). The atrophic nature of the uterus was similar to the report by Kholkute et al. (1976) in rats treated with *Hybiscus rosasinensis* L. extract.

In general the drug treatment caused significant damage to the histoarchitecture of the female system. Ovulation is a complex process, initiated by the surge of luteinizing hormone (LH), and is characterized by resumption of meiosis and restructuring of the follicular wall, resulting in follicular rupture and the release of a mature fertilizable ovum (Guraya & Dhanju, 1992). The effect of the *Physalis* extract treatment and the above mentioned changes in the histoarchitecture, absence of corpora lutea, follicular irregularities and ovary weight changes, may be due to: 1. Inhibition of synthesis and/or release of gonadotrophins from the pituitary, 2. Direct inhibitory effects on ovaries, uterus and oviduct, and 3. The inactivation of circulating gonadotrophins as noted earlier by Kalra and Prasad (1967). From the present study it is evident that oral administration of the petroleum ether extract of *P. minima* causes alterations in the histoarchitecture of the female reproductive system and has inhibitory effects of transient nature, since the cyclicity of the rats recovered following withdrawal of the drug.

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