TIMELY ADMINISTRATION OF EXTRACT OF FERULA JAESCHKEANA CAUSES LUTEOLYSIS IN THE OVARY OF CYCLIC GUINEAPIG

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Abstract: Effect of hexane extract of Ferula jaeschkeana has been studied on corpora lutea of adult cyclic guinea-pigs. Administration of extract showed duration dependent luteolytic changes in the corpora lutea. Its administration for first three days from the onset of estrus caused significant decrease in the diameter of corpora lutea in the ovary at day 10 of cycle. Ovarian wet weight, proteins and glycogen contents were decreased while the activity of acid phosphatase in the ovary was increased. These luteolytic changes in the ovary have also been observed in the histological findings. Administration of extract for other durations (4-6, 7-9 or 10-12 of cycle) did not cause any change at 10th and 16th day.

Key words: Ferula Jaeschkeana guinea pig luteolytic cyclic

INTRODUCTION

Phytoestrogens are naturally occurring estrogens found in variety of plants or foodstuffs, which may be ingested directly or as constituents of the tissues of animals that ingest the plant sources. Phytoestrogens have a few propitious effects, the majority of the affects are nocuous. Most of them have also been reported to impair fertility in domestic animals and also disturb normal gestation. There are number of phytoestrogenic plants which may be consumed by humans and Ferula jaeschkeana is one of them. It is commonly known as "Heeng" (family: Umbelliferae) and has received attention concerning its antifertility activity (1). Besides other therapeutic uses (2), antifertility activity due to estrogenic action has been reported in its hexane extract (3). As estrogenic substances influence female reproductive organs, efforts have been made to assess the effect of hexane extract of Ferula jaeschkeana on the corpora lutea of the ovary of the cyclic guinea-pig.

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group A received oral administration of the hexane extract for 3 days (day 1-3 and 4-6 separately) while animals of group B received oral administration from day 7-9 and day 10-12 separately. The animals of groups A and B were sacrificed on 10th and 16th day of cycle respectively. For each set parallel controls were maintained which received vehicle only. Vaginal smear of all animals were examined daily. At autopsy, the ovaries of each animal were excised and then weighed to the nearest of mg and processed for estimation of proteins (4), glycogen (5), acid and alkaline phosphatase activity (6). One of two ovaries of each animal were fixed in Bouin's fluid for routine histology. Serial sections at 10 𝜇 were cut and stained in haemotoxylin-eosin and examined microscopically. Each corpus luteum was measured in its largest section with ocular micrometer; the maximum diameter, and a diameter at right angles to it were determined. The mean diameter was an average of the two measurements. Ovarian wet weight and various biochemical parameters were studied in treated groups and compared with those of the respective controls. The results were statistically analysed using Students' 't' test.

RESULTS

Fig. 1 reveals that the administration of the extract for 3 days (1-3 days from the onset of estrus stage) significantly decreased the mean diameter of the corpora lutea at day 10 of autopsy when compared with control (P<0.05). In animals fed extract from 4-6 days, 7-9 days and 10-12 days of estrus cycle no significant decrease in the diameter of corpora lutea was observed.

![fig1](image)

**TABLE I:** Effect of oral administration of hexane extract of *F. jaeschkeana* in a dose of 25 mg/kg on various parameters of ovary of adult cyclic guinea-pig.

<table>
<thead>
<tr>
<th>Group</th>
<th>Days of treatment</th>
<th>Day of autopsy</th>
<th>Treatment</th>
<th>Wet weight (mg/100 g)</th>
<th>Protein (mg/100 mg)</th>
<th>Glycogen (mg/100 mg)</th>
<th>Acid phosphatase (mg P/100 g/hr)</th>
<th>Alkaline phosphatase (mg P/100 g/hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>1-3</td>
<td>10</td>
<td>C</td>
<td>9.8 ± 0.42</td>
<td>18.9 ± 0.97</td>
<td>132.3 ± 6.94</td>
<td>120.0 ± 10.2</td>
<td>330.5 ± 26.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>E</td>
<td>7.1 ± 0.36*</td>
<td>16.1 ± 0.86*</td>
<td>102.4 ± 5.19</td>
<td>176.1 ± 12.8*</td>
<td>314.2 ± 25.1</td>
</tr>
<tr>
<td></td>
<td>4-6</td>
<td>10</td>
<td>C</td>
<td>9.6 ± 0.60</td>
<td>19.2 ± 1.50</td>
<td>130.2 ± 8.4</td>
<td>122.3 ± 9.62</td>
<td>315.1 ± 25.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>E</td>
<td>8.8 ± 0.62</td>
<td>21.4 ± 1.79</td>
<td>148.2 ± 11.8</td>
<td>131.7 ± 10.5</td>
<td>365.7 ± 29.2</td>
</tr>
<tr>
<td>B</td>
<td>7-9</td>
<td>16</td>
<td>C</td>
<td>6.6 ± 0.32</td>
<td>15.1 ± 1.20</td>
<td>105.1 ± 8.4</td>
<td>170.9 ± 13.6</td>
<td>323.3 ± 25.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>E</td>
<td>7.5 ± 0.30</td>
<td>16.3 ± 1.30</td>
<td>126.6 ± 10.1</td>
<td>157.4 ± 12.5</td>
<td>341.2 ± 27.2</td>
</tr>
<tr>
<td></td>
<td>10-12</td>
<td>16</td>
<td>C</td>
<td>6.2 ± 0.39</td>
<td>15.5 ± 1.24</td>
<td>111.0 ± 8.88</td>
<td>165.2 ± 13.2</td>
<td>320.6 ± 25.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>E</td>
<td>7.2 ± 0.37</td>
<td>16.6 ± 1.32</td>
<td>123.7 ± 9.89</td>
<td>152.9 ± 12.2</td>
<td>345.0 ± 27.6</td>
</tr>
</tbody>
</table>

*P vs Control <0.05
glycogen contents and increased acid phosphatase activity (P<0.05 for each). Administration on 4-6, 7-9 or 10-12 days of estrus did not significantly change wet weight of ovary and other biochemical parameters.

Histological examination revealed that the ovary of control cyclic guinea pig at day 10 of estrus cycle was composed of well developed corpus luteum and the luteal cells were enlarged and appeared secretory (Fig. 2). Administration of hexane extract for 3 days (1-3 of estrus) and autopsied on day 10 showed early signs of regression of corpus luteum. These include foamy appearance of cytoplasm, reduced cytoplasmic ratios, absence of mitotic figures, pyknotic nuclei and disappearance of arrangement of luteal cells into columns and loss of discrete boundaries (Fig. 3). Administration of the extract on day 4-6 of estrus showed the presence of Graafian follicles at the periphery and also developed corpus luteum. The mean diameter of the corpus luteum of treated guinea-pig (1.73±0.13 mm) did not differ significantly from the control (1.87±0.14 mm). Further the signs of regression were apparent in the corpora lutea of control animals at day 16 of estrus cycle (Fig. 4). It includes the reduction in size of the corpora lutea (0.70±0.88 mm). Normal Graafian follicles were absent in these ovaries. At day 16 of cycle, the corpora lutea of animals receiving hexane extract of F. Jaeschkeana for 7-9 and 10-12 days did not show any regression when compared to control. Vacuolization of luteal cells was less, corpus luteum became a compact structure mainly by hypertrophy of luteal cells, and an invasion of the centre by connective tissue was observed.

**DISCUSSION**

Mammalian ovary undergoes cyclic changes which are regulated by the hormones of hypothalano-hypophysial axis. Timely events in the ovary of animals having longer period of
estrus cycle are more conspicuous. In the
Guinea-pig the normal estrous cycle ranges from
16 to 17 days of length with 16 days dominance.
The corpora lutea during this period undergoes
morphological and functional alterations related
to the timings after the onset of estrus. Day 1 of
estrus cycle is designated on the basis of
complete cornification of vaginal smear. It is
well known that corpora lutea of cyclic guinea
pig grows in size due to the hypertrophy and
hyperplasia of luteal cells between day 3 and 10
of the cycle and regression starts on day 12
which continues till day 16 of cycle. In contrast
to that in rats, the hypertrophy and regression of
corpora lutea in guinea pig has been reported
due to the alteration of contents of progesterone
(7). The role of estrogen in the regression of
corpora lutea has also been described (8). On
the contrary in other species like rat it is the
estrogen which stimulates or releases pituitary
luteotrophin feed back (9). The difference in the
response of estrogen in two species may be
related to the hypothalamic-hypophysial axis as
well to the difference in the release of hormones
maintaining corpora lutea (10). In our study,
the hexane extract of F. jaeschkeana caused
luteolytic effect on the corpus luteum in the
ovary of cyclic guinea-pig, however, it did not
cause any effect on the follicular development.
Similar results have been shown with exogenous
administration of estrogen in early days of
estrus cycle (11). Aldred et al (12) reported
that progesterone administered to cyclic guinea-
pigs caused partial destruction of corpora lutea.
Regression of corpus luteum under the effect of
hexane extract of F. jaeschkeana when
administered for first 3 days of cycle has also
been confirmed with the decrease in ovarian
weight and some biochemical constituents
like protein and glycogen.

The exact mechanism by which hexane
extract of F. jaeschkeana caused luteolysis in
the ovary of cyclic guinea-pig is not known but
it is assumed that the estrogenic nature of
extract is mainly involved. It is because in other
species such type of estrogen dependent effect
is known. In cyclic cow when estrogen is
administered before day 10 but not after day 15
of cycle caused luteal regression (13). In the
pregnant hamster it is effective only when
administered before day 4 of pregnancy (14). It
is interesting to note that hexane extract of F.
jaeschkeana caused luteolysis only when
administered during first 3 days of the onset of
cycle. It is also known that hypertrophy and
hyperplasia of luteal cells starts after 3 days.
Therefore, it is assumed that some anti-
luteotrophic factors appear after day 3 of the
cycle which inhibit luteolysis. The maintenance
of corpora lutea of guinea pig by exogenous
supply of individual pituitary hormones (7, 12)
has failed. Therefore, it is pointed out that the
luteal maintenance/regression in the guinea-pig
may be dependent on the interactions between
the hexane extract of F. jaeschkeana and a
pituitary hormonal complex, rather than a single
hormonal factor.

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