Effects of *Achillea Millifolium* extract consumption by pregnant mice on pregnancy outcome and reproductive system of their female offspring

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Abstract:

**Background:** *Achillea millefolium* (*Yarrow*) is medicinal plant that is traditionally used against inflammatory and spasmodic gastrointestinal compliant.

**Objective:** To study the effect of the consumption of *Achillea* extract by pregnant mice on pregnancy outcome and on the reproductive system of the female offspring.

**Materials & Methods:** 70 adult pregnant female mice at age of 40-45 days were used in this study. These 70 mice were divided equally into two groups: experimental group (G1) and control group (G2). The experimental group was given 1mg/kg body weight/1ml of D.W of *Achillea millefolium* extract orally during 3 weeks of pregnancy, while the control group was given 1ml of D.W orally alone and for the same period.

After delivery the number and weight of the litters were recorded. 40 days after delivery, the weight of the female reproductive system was estimated, histological sections were done for the ovaries and oviducts, their diameters were measured, in addition serum was taken from these mice and measurement of FSH, LH and $E_2$ was done for both groups.

**Results:** The results of the experimental group showed highly significant decrease in litter size and significant decrease their weight. In addition young females born from treated mothers showed significant decrease in the weight of reproductive system, diameter of ovaries and diameter of oviducts. Also, significant decrease was noticed in the level of FSH, LH and Estradiol level in the experimental group.

**Conclusion:** Consuming of *Achillea millifolium* extract during pregnancy will produce bad effect on the pregnancy outcome in addition to bad effect on the reproductive system of the female offspring.

**Key words:** *Achillea millifolium*, reproductive organs, hormones.
Introduction:

There is perhaps no function more important in life than reproduction of the species. The exposure of pregnant mothers to toxic chemicals as well as to drugs that can be prescribed during pregnancy can exert toxic effects on the mother which can also mean exposure of the fetus as a result of circulating blood through the Placenta (1).

The use of medicinal herbs among the general population gives rise to the possibility of therapeutic or toxic effect in patients seeking conventional medical assistance (2). Different species from the *Achillea millefolium* L. (Asteraceae) aggregate are used in traditional European medicine against gastrointestinal and hepato-biliary disorders due to their spasmyloytic and antimicrobial properties (3). The recommended human dose is 50 mg/kg/day (4). It is popularly known as “yarrow”, and it is widely distributed medicinal plant that has...
been used for over 3000 years (5). Popular indications of this specie include treatment of wounds, hemorrhage, headache, inflammation, pain, spasmodic diseases, flatulence, and dyspepsia (6).

A review on the chemical constituent of *Achillea millefolium* was published recently and the following compound classes were reported as metabolites: Trepenoids, lignans, flavonoids & amino acid derivatives (7). Flavonoids have been demonstrated to have both estrogenic and antiestrogenic activities (8). As a result, yarrow has been used as an abortifacient by some ethnic groups (9), as a contraceptive (10), a stimulant for uterine contractions and to cure amenorrhea (11).

**Materials & Methods:**

Seventy mature females (Swiss Webster) mice of 40-46 days age were used in this study. They were put in control cage under standard condition of temperature and illumination cycle (12 hr dark and 12 hr light), and free access to water and food.

Each proestrus female mouse was mated with one male mouse overnight. The presence of sperm in an estrus vaginal smear in the next morning was taken as evidence of mating. The day of positive smear was designated as day 0. Then these mice were divided into two equal groups: experimental (G1) and control (G2) groups. The experimental group was treated with 1gm/kg body weight of alcoholic extract *Achillea millefolium* dissolved in 1ml of distilled water orally for three weeks during pregnancy, while the control group was fed with distilled water only by the same volume and period that used with experimental group. The number and body weight of all litters of both groups were recorded. Forty days later (about puberty age), the female animals were sacrificed to get their reproductive system out, weighing of these organs was done for both groups, then ovaries and oviducts were taken, the fixed histological sections with thickness of 5 µm were prepared using the routine histological technique (12), ovarian diameter, as well as the diameter of the oviduct were measured. In addition blood samples were taken to measure the levels of FSH, LH and Estradiol hormones.

**Results:**

1- Effect of *Achillea millefolium* on pregnancy outcome: When comparison was done for the birth rate and weight of the litters in the experimental and control groups, highly significant (p<0.01) difference in the birth rate was noticed in the experimental group result and significant (p<0.05) difference in their weight in comparison to control group (table-1-).
Table (1): Effect of *Achillea Millifolium* on birth rate and body weight of the mice offspring.

<table>
<thead>
<tr>
<th>parameters</th>
<th>Experimental group (G1)</th>
<th>Control group (G2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth rate</td>
<td>3.7 ** ±0.016</td>
<td>8.3 ±0.023</td>
</tr>
<tr>
<td>Body weight</td>
<td>15.4* ±0.06</td>
<td>18 ±0.08</td>
</tr>
</tbody>
</table>

*significant (p<0.05) difference.*  
**Highly significant (p<0.01) difference.**

2- Effect of *Achillea Millifolium* on weight of reproductive organs:  
A significant (p<0.05) difference in the weight of reproductive organs of female offspring was noticed in the experimental group compared to control group (table-2).

Table (2): Effect of *Achillea Millifolium* on the reproductive organs' weight of female offspring.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Experimental group G1</th>
<th>Control group G2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight of reproductive system</td>
<td>3.1* ±0.03</td>
<td>4.2 ±0.04</td>
</tr>
</tbody>
</table>

*Significant (p≤0.05) difference.*

3- Effect of *Achillea millifolium* on histology of reproductive organs of the mature offspring:  
Table (3) show the changes in the histology of ovaries (Pic.1 and 2) and oviducts (Pic. 3and 4) of female offspring after administration of *Achillea millifolium* to the mothers. Significant decrease (p<0.05) in the diameter of the ovaries and diameter of the oviducts were recorded in the experimental compared to control group.

Table (3): Effect of *Achillea Millifolium* on the diameter of ovary and oviduct of female offspring.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Experimental group G1</th>
<th>Control group G2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diameter of ovary</td>
<td>18* ±0.07</td>
<td>20 ±0.1</td>
</tr>
<tr>
<td>Diameter of oviduct</td>
<td>7* ±0.01</td>
<td>9 ±0.02</td>
</tr>
</tbody>
</table>

*Significant (p≤0.05) difference.*
Figure (1): The ovary of mature female mice from controlled group.

Figure (2): The ovary of mature female mice from the experimental group.
Figure (3): The oviduct of mature female mice from control group.

Figure (4): The oviduct of mature female mice from the experimental group.

4- **Effect of *Achillea millifolium* on reproductive hormones of the mature offspring**: When the results of the reproductive hormones (FSH, LH and Estradiol) of both groups was compared, significant decrease (p<0.05) was found in the levels of these hormones in the experimental group compared to control group as shown in table (4).
Table (4): The effect of *Achillea Millifolium* on reproductive hormones of female offspring.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Experimental group G1</th>
<th>Control group G2</th>
</tr>
</thead>
<tbody>
<tr>
<td>FSH</td>
<td>3.3* ±0.02</td>
<td>4.8 ±0.03</td>
</tr>
<tr>
<td>LH</td>
<td>1.7* ±0.01</td>
<td>2.3 ±0.02</td>
</tr>
<tr>
<td>E₂</td>
<td>5* ±0.023</td>
<td>6.3 ±0.03</td>
</tr>
</tbody>
</table>

*Significant (p≤0.05) difference.

**Discussion:**

Herbal medicines have become a popular form of therapy in many countries. Even though they are often prompted as natural and therefore harmless, medicinal plants are by no means free from toxicity (13, 14). The present study was undertaken to evaluate the female reproductive toxicity of the aqueous extract of *A. millefolium* leaves.

In this study the litter size (birth rate) showed highly significant decrease for the mothers which received *Achillea* extract than those which were given D.W. only and this result does not agree with previous studies (11) and may assist the previous thoughts of *yarrow* as an abortifacient plant (15), and causing uterine contraction (16). The decrease in the birth rate may be explained to be due to the decrease in estradiol levels that may hamper ovulation, preparation of the reproductive tract for zygote implantation, and the subsequent maintenance of the pregnancy state (17, 18).

Also the present study showed a significant decrease in the body weight of the young females born from *achillea* extract treated mothers; this suggests that there is inadequate nutrient transfer across the placenta to the fetus (19). The spasmolytic action of some of the chemicals present in yarrow (*Achillin, apigenin, and luteolin*) may contribute to the decrease in fetal weight because they were shown to reduce gastrointestinal spasm and this reduction in motility may inhibit the absorption of nutrients into the maternal bloodstream, reducing the availability of nutrients for placental transfer to the fetus, thus reducing the fetal weight (20, 21). These results agreed with that recorded in the previous studies (22, 23).

In addition the effect of *Achillea* extract was studied on ovaries and oviducts. Oviducts are dynamic organs that support gamete transport, maturation, fertilization, early embryonic growth and development, and the timely transport of embryos.
for implantation in the uterus. Oviducts are targets of estradiol and progesterone produced in response to FSH and LH stimulation of ovaries (24). In this study significant decrease in the level of FSH, LH and Estradiol hormones are noticed. These hormonal imbalances may be caused by numerous chemical agents contained in plant extracts. Phytochemical screening has revealed many bioactive as well as toxic agents of plant extracts that can affect the regulation of oestrous cycle, conception and reproduction (25, 26). Alkaloids and flavonoids have been shown to reduce plasma concentrations of LH, estradiol and FSH (27, 28). It is possible that the extract might have exerted its effect on the anterior pituitary or the hypothalamus since the secretion of FSH is regulated by the gonadotropic releasing hormone secreted by the hypothalamus (29). Thus, the reduction in the serum concentration of estradiol observed in this study may be attributed to a decreased aromatase activity or substrate supplementation during estrogen synthesis (30). In addition it is well established that estradiol is directly responsible for the growth and development of reproductive organs (31), so that a significant decrease in diameter and weight of the ovaries in the experimental group was noticed.

Conclusion:

Achillea millefolium consumption in a dose of 1 gm during pregnancy cause significant decrease in number and body weight of the offspring in addition to significant decrease weight of the reproductive organs, diameter of ovaries and oviducts in addition to its lowering effect on reproductive hormones FSH, LH and E2.

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References:


5- Mitich L.W. Intriguing World of Weeds: Yarrow –the herb of


20- Hadley M.E. Hormones and female reproduction physiology. In:


