Effects of Methomyl on the biochemical and reproductive parameters in pregnancy rats: The protective role of Pistacia Lentiscus oil.

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INTRODUCTION

Carbamates class is one of the most common used pesticides in some field of applications as insecticides, herbicides and fungicides. Among carbamates, **methomyl (MET)** is one of carbamate insecticides used in agriculture to control a broad spectrum of insects and arthropods in fruits, cotton, soybeans, vegetables and other field crops, on turf and in livestock facilities.). It is classified as restricted use pesticide because it's highly hazardous to humans and mammals (EPA, 1998a). However, until now, it is remain used in developing countries and little is known about its effects on female reproductive system and outcomes.

***Pistacia lentiscus* L (PL)**. is a green shrub belonging to the Anacardiaccea family, natively distributed in the Mediterranean countries such as north Algeria. It is classified as medicinal plant which is used since the antiquity in traditional medicine for the treatment of various kinds of diseases like eczema, inflammation, hypertension, hypercholesterolemia, and gastric disorders (Djerrou , 2014; EMA, 2015).

Hence, in this study, we attempt to explore the effects of **methomyl** on the biochemical and reproductive parameters and the possible protective role of ***Pistacia lentiscus oil* (PLO)** against MT- induced toxicity in pregnant rats.

MATERIAL AND METHODS

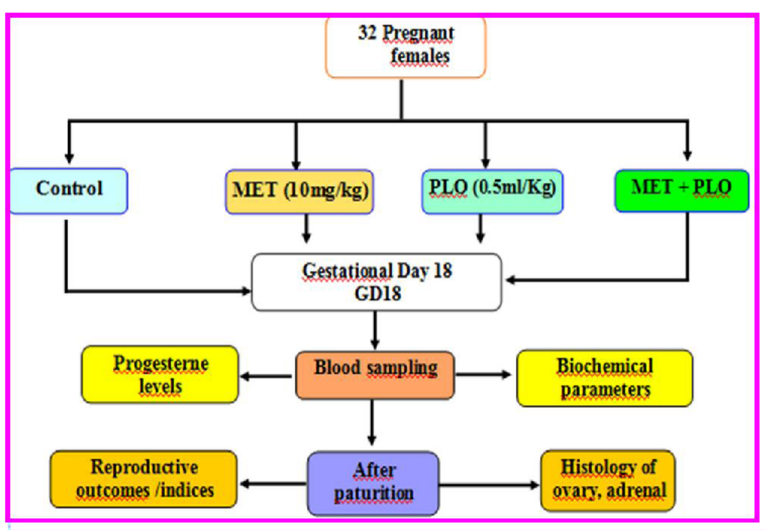


Table 1. The effects of Methomyl (MET), *Pistacia lentiscus* oil (PLO), and their combination (MET +PLO) on body weight gain (BWG, g %), relative weight of adrenal (ARW × 10-1, g %) and ovary (ORW, g %), food intake (FI, g/day) and water consumption (WC, ml/day) after 18 days of treatment.

Parameter	Groups			
	Control	MET (10mg/kg)	PLO(0.5ml/Kg)	MET + PLO
Initial body weight GD0	235±5.88	206±8.22	190.25± 6.42	219.37±4.89
Final body weight GD18	292.5± 17.03	240.51±8.17	248.12±8.35	275± 7.02
BWG	57.75±12.98	34.87± 1.78*[a]	57.87±8.23	52.62± 8.37*[b]
ARW	0.012± 0.008	0.022±0.01	0.018±0.013	0.020±0.012
ORW	0.021±0.002	0.025±0.0003	0.03±0.002	0.024±0.001
FI	21.72± 1.42	19.48±1.56*[a]	23.48±0.47	23.52± 0.35
WC	29.45± 2.69	25.12± 0.74	30.01± 0.84	29.56± 0.88

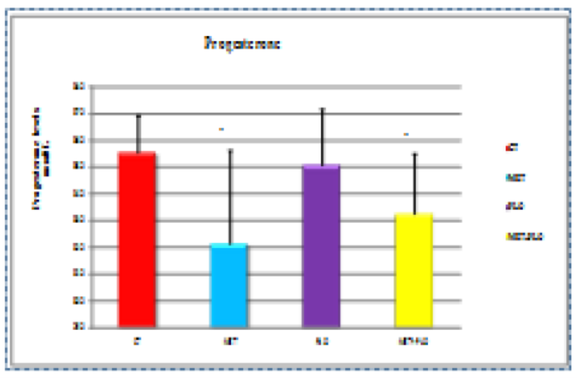
Table 2. The effects of Methomyl (MET), *Pistacia lentiscus* oil (PLO), and their combination (MET +PLO) on reproductive outcomes in pregnant female rats after post-partum.

Parameter	Groups			
	Control	MET (10mg/kg)	PLO (0.5ml/Kg)	MET + PLO
Live litter size (%)	100	83.33	87.5	85.71
Newborn mean weight. (g)	5.57 ± 0.25	4.61 ± 1.11*[a]	5.3 ± 0.70	4.70 ± 0.95
Sex ratio (M/F %)	100	61.53*[a]	72.41	78.57
Gestation index (%)	100	100	100	100
Viability index (%)	100	94*[a]	98	97.61

Table3. The effects of Methomyl (MET), *Pistacia lentiscus* oil (PLO), and their combination (MET +PLO) on

Parameter	Groups			
	Control	MET (10mg/kg)	PLO(0.5ml/Kg)	MET + PLO
Cholesterol(g/l)	1.53 ± 0.026	1.98 ± 0.331***[a]	1.50 ± 0.012**[a]	1.53± 0.006***[b]
Glucose (g/l)	0.81 ± 0.012	1.64 ± 0.535***[a]	0.86 ± 0.005	0.75 ± 0.017***[b]
Creatinie (mg/dl)	4.20 ± 0.065	4.65± 0.302***[a]	4.16 ± 0.047	4.40 ± 0.155***[a]/*[b]
Urea (g/l)	0.41 ± 0.002	0.50 ± 0.02**[a]	0.41 ± 0.004	0.48 ± 0.003
Total protein (g/dl)	8.09 ± 0.005	7.81± 0.138*[a]	8.15 ± 0.022**[a]	7.93 ± 0.008
ASAT (U/l)	20.88±0.638	23.44 ± .445***[a]	20.52 ± 0.295	23.52 ± 0.291***[a]
ALAT (U/l)	78.94±0.507	81.19± 1.078*[a]	79.76 ± 0.449	80.04 ± 0.471

Fig.1. The effects of Methomyl (Met), *Pistacia lentiscus* oil (PLO) and in combination (Met +PLO) on progesterone levels in GD18 of pregnant female rats.



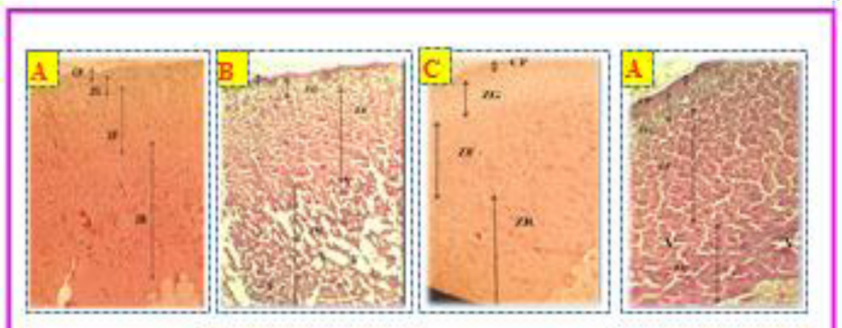


Fig. 2. Histology of adrenal gland showed Glomerular (ZG), Fascicular (ZF) and Reticular (ZR) zones of cortex and Medulla of Control group (A), Methomyl (B), *Pistacia lentiscus* oil (C) and in combination (D) treated dams from GD0 to GD18. The sections were stained with Hematoxylin-Eosin and magnification 40x, V: vacuolization.

Fig. 3. Photomicrograph of ovary sections of control (A) and *Pistacia lentiscus* oil (C) groups in which many different stages of developing follicles were observed, , primary follicle (a), secondary follicle (b), antral follicle (c), graffian follicle (d), corpus luteum (e) . In methomyl (B) and methomyl plus *Pistacia lentiscus* oil (D), many degenerative follicles, a lot of atretic follicles in different stages (c1, d1, e1) . Coloration H&E and magnification 40x.

Results are represented in tables **(1, 2, 3)** and figures **(1, 2, 3).** All values are given as mean ± SM; statistically significant different from control group are ([a]*P<0.05; [a]**P<0.01; [a]***P<0.001), also statistically significant different from methomyl group are ([b]*P<0.05; [b]**P<0.01; [b]***P<0.001).

In this study, MET reduces significantly the body weight gain and food intake, and increased the levels of biochemical markers (cholesterol, glucose, creatinine, urea, ASAT , ALAT and total protein). In addition, MET induced reproductive toxicity pronounced by a decline in litter size, the mean weight of newborn, sex ratio, viability and progesterone levels.

The hispathological examinations revealed that MET induces tissue damage in the adrenal gland marked by cells disorganization and vacuolization, as well as an obvious degenerative changes in ovary structure marked by a few number of healthy follicles and many cystic and atretic follicles at different stages of development.

Pistacia lentiscus group exhibit a similar pregnancy outcomes and histological structure in adrenal gland and ovary organs when compared with control, however a modest elevation in progesterone level was marked.

Also the co-administration of *Pistacia lentiscus* oil along with MET can alleviate and restore partially or completely some toxic effects induced by MET during the treatment period.

DISCUSSION AND CONCLUSION

Pesticides became one of the essential products in agriculture to control pests and increase crop yields. Animal and human exposure to these products has been strongly associated with many health problems (Bhardwaj and Saraf, 2014; Oheme and Mannala, 2001), including carcinogenesis, neurotoxicity, diabetes, endocrine disruption, reprotoxic effects such as infertility, stillbirth, premature birth, low birth weight, ovarian disorders and changes in sexual behavior (Henderson et al., 1995; Schettler et al., 2003; Andersson et al., 2014).

Our results show a reduction of body weight and daily food intake and a significant increase of cholesterol, glucose, creatinine, urea, ASAT, ALAT. These results are in consistent with that reported by Al Shinnawy (2008), Grag *et* al. (2009) and El- Demerdash (2013).

Also, we noted histological changes in the ovaries of female rats treated with MET marked by loss of follicles and an increase in atretic and cystic follicles. These results confirm that obtained in several previous studies (Boseilla et al., 1981. Matter et al., 1981. Watermann et al., 2008; Mokhtar et al., 2013). Furthermore, MET caused degenerative and vacuolation aspect in the zona fasciculata of adrenal cortex. .

Moreover, as shown in fig 1. and table 2. the alteration in the pregnancy outcomes (litter size, sex ration, viability and body weight of newborns) and progesterone levels by MET is in agreement with other studies (Kumar et al., 2011; Mokhtar et al., 2013)

Pistacia lentiscus oil supplementation with MET can ameliorate or adjust to normalcy all pregnancy outcomes progesterone levels and histopathological changes in adrenal and ovary induced by MET confirming its protective effect against MET toxicity. This preventive role may be due to its potential antioxidant, cytoprotective, anti-inflammatory and anticancer activities (Remila et al., 2015).

In conclusion, MET induces biochemical changes, reproductive and histopathological effects on ovary and adrenal glands, while *Pistacia lentiscus* protects efficacy against MET-induced toxicity in female pregnant rats.

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