

ORIGINAL ARTICLE

Thyroid retarding effects of dimethyl sulfoxide

Ismat Fatima[1,*], Munawar Ali Munawar[2], Affia Tasneem[1], Nasir Mehmood[1]

[1]CENUM, Mayo Hospital, Lahore
[2]Institute of Chemistry, University of the Punjab, Lahore

Abstract

Aims The study was aimed to determine the antithyroid activity of Dimethyl sulfoxide, a universal solvent.

Methods The antithyroid effects of DMSO were investigated *in vivo* on male Wistar rats.

Results Daily dose administration of 0.4 mL/100g to the animals significantly decreased the free triiodothyronine and thyroxine levels and increased the thyroid stimulating hormone levels. The animals were afterwards dissected and thyroids were studied under microscope which revealed modifications at cellular level. Thyroid weight per 100 grams of body weight for the animals treated with DMSO were also found higher than control animals.

Conclusion DMSO demonstrated moderate antithyroid activity in rats.

***Key words**: Antithyroid activity, Dimethyl sulfoxide, histology, in vivo activity*

***Correspondence**

Ismat Fatima
Centre for Nuclear Medicine
Mayo Hospital Lahore
G.P.O Box No. 53
Tel: +92-42-99214433
Fax: +92-42-99214432
Email: ismat_rehan@yahoo.com

Introduction

Dimethyl sulfoxide (DMSO) is an important polar aprotic solvent that dissolves both polar and nonpolar compounds and is miscible in a wide range of organic solvents as well as water [1]. It is a colourless liquid, which readily penetrates the skin and has garlic like taste. Its medicinal properties are not new but thousands of articles have been published evaluating its importance since 1963, when Stanley Jacob and his team at the University of Oregon discovered that DMSO can penetrate the skin and other membranes without damaging them and could carry other compounds into a biological system [2]. Soon after this discovery, Dr. Jacob started working on the medicinal properties of Dimethyl sulfoxide and devoted rest of his life to this research.

In spite of the controversies which have subsequently arisen, DMSO is being used as a topical analgesic, a vehicle for topical application of pharmaceuticals, as an anti-inflammatory [3] and an antioxidant. Because DMSO increases the rate of absorption of some compounds through organic tissues including skin, it can be used as a drug delivery system. It is used in antifungal medicines enabling them to penetrate the skin and nails [4].

Hammerman and Ritterman [5] have studied the effects of DMSO on frog tadpoles and observed that 1% v/v solution causes tail

 2221-0288(201201/01)1:1<33:TREODS>2.0.TX;2-M

shortening and delay in the metamorphosis of frog tadpoles. They found that a possible antithyroid activity occurs in DMSO.

Present work deals with the possible antithyroid action of DMSO in male Wistar rats. DMSO was administered to the rats via *i.p.* injections and its effect on serum hormone levels as well as thyroid histology was determined. Although we are not able to present DMSO as an alternate medicine for hyperthyroidism at this stage but may be afterwards when controversies regarding safer use of DMSO are resolved, it may be considered for the treatment of hyperthyroidism also.

During three different experiments aimed to determine the medicinal effects of certain compounds DMSO was employed as solvent (vehicle). The radioimmunoassay (RIA) to determine the concentrations of free T3 and T4 in the blood serum of the control animals and those of treated with DMSO, exhibited that the latter category showed a relative hormonal decrease than the former. The histological study of thyroid sections also revealed a difference between the follicular epithelium of the control and the vehicle treated animals. Similarly, the TSH levels measured with ELISA method, demonstrated a relative increase of this hormone in DMSO treated animals than the control animals. The animals were administered with daily dose of 0.4mL/100g of DMSO via *i.p.* injections for 15 days. Though data scarcely exceeded significance level ($\alpha = 0.05$) yet it was consistent enough to further evaluate DMSO from this particular view point [3, 4]. Therefore, a separate experiment was designed and effects of DMSO in male Wistar rats were evaluated by increasing the dose rate as well as treatment time.

Materials and methods

DMSO of spectroscopic grade was obtained from Merck. It was dried over calcium hydride, distilled under reduced pressure and stored over type 4A molecular sieves and used without further purification for *in vivo* study. Free T_3 and T_4 kits of Immunotech (France) and rat TSH ELISA kit from Cusabio Biotech Co. Limited (China) were used.

In vivo studies

The *in vivo* study was performed on young male Wistar rats of 125 to 200 g weight. Total four experiments were performed in this regard. In the first three experiments which were in fact aimed to study the medicinal effects of certain organic compounds, the animals were divided into control, vehicle control, treated groups [6,7]. In these experiments the control and vehicle control groups comprising of 5 animals each, obtained 0.2 mL/100g dose of normal saline and DMSO respectively for fifteen days, daily in the morning via *i.p.* injection. While, in the fourth experiment, which was particularly designed to study the antithyroid effects of DMSO, the same number of animals (n = 5) each for control and DMSO treated groups were administered with 0.4 mL/100g normal saline and DMSO respectively daily in the morning for 21 days.

The animals were fed with chick feed with water *ad libitum*. The animals were weighed before sampling and blood samples were collected from all animals by puncturing abdominal aorta under light diethyl ether anesthesia. Standard animal protocols were adopted for the experimentation. Free T_3 and T_4 levels were determined using *radio immunoassay* technique, while that of TSH with *ELISA* method.

Histological studies

The animals (one from each group) were sacrificed afterwards on the same day under deep diethyl ether anesthesia and thyroid glands were removed for histological studies. The dissected thyroid from each animal was placed in Petri dishes containing saline solution to clear organ from fats and blood. The weight of thyroid was determined with sartorius balance to calculate "thyroid body index", which is defined as the weight of the

Table 1 Mean hormonal concentrations of control and DMSO treated animals

Assay Results	Control			DMSO Treated		
	FT_3 (pmol/L)	FT_4 (pmol/L)	TSH (µi.u./mL)	FT_3 (pmol/L)	FT_4 (pmol/L)	TSH (µi.u./mL)
[a]**Experiment I**	9.74±0.86[c]	37.56±4.16	1.86±0.63	8.41±1.12	33.51±3.94	2.04±0.35
[a]**Experiment II**	8.42±1.21	36.06±3.64	1.56±0.44	8.15±1.36	34.09±4.09	1.7±0.39
[a]**Experiment III**	9.68±1.19	38.42±2.39	1.88±0.26	9.07±1.29	37.19±2.80	1.96±0.23
[b]**Experiment IV**	10.13±0.91	41.27±3.07	1.48±0.31	7.95±1.01	30.83±3.51	2.19±0.29

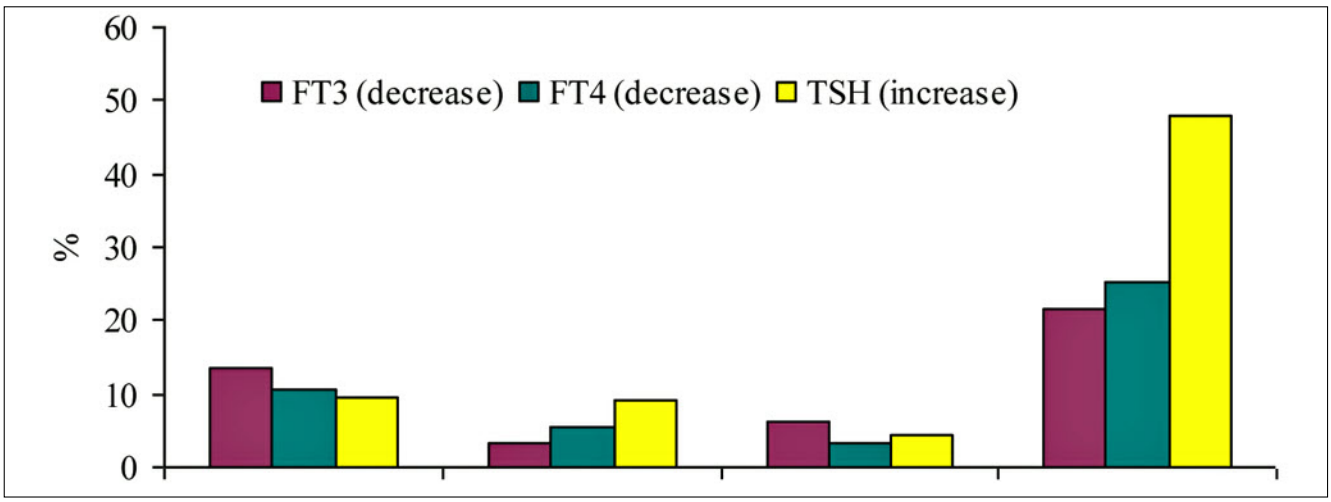

Figure 1 *Mean percentage hormonal variations with respect to control*

of thyroid per 100 gram of final body weight. The tissues were then fixed in 4% PFA for 4-6 hours. Haematoxylin and Eosin stains were used for staining. Five µm thin sections of thyroid were studied under Olympus BX51 microscope fitted with Olympus DP12 digital camera at 20 and 60 µm magnifications. Slides of all groups were photographed and changes at cellular level were noted.

Results and Discussion

Radioimmunoassay results of all four experiments showed decrease of free T_3 and T_4 concentrations in the serum of animals treated with DMSO compared with the control group. Similarly, the TSH levels measured with ELISA method demonstrated a relative increase of this hormone in DMSO treated animals than in the control animals (Table 1). The data scarcely exceeded significance level (a = 0.05) in first three experiments but for 4th experiment in which the dose as well as treatment time were increased, significant variations ($a \leq 0.05$) in all three hormones were recorded. The percentage hormonal variations in the DMSO treated group with respect to control showed the medicinal/antithyroid effects to be dependent on the dose and time (Figure 1).The histological study of thyroid sections also revealed the difference between the follicular epithelium of control and DMSO treated animals (Figure 2). Mild to moderate follicular hypertrophy and hyperplasia was observed along with consumption of colloid. A transition of epithelium from cuboidal to cylindrical also exhibits the hyperactive condition of the gland thus demonstrating moderate antithyroid effects of DMSO.

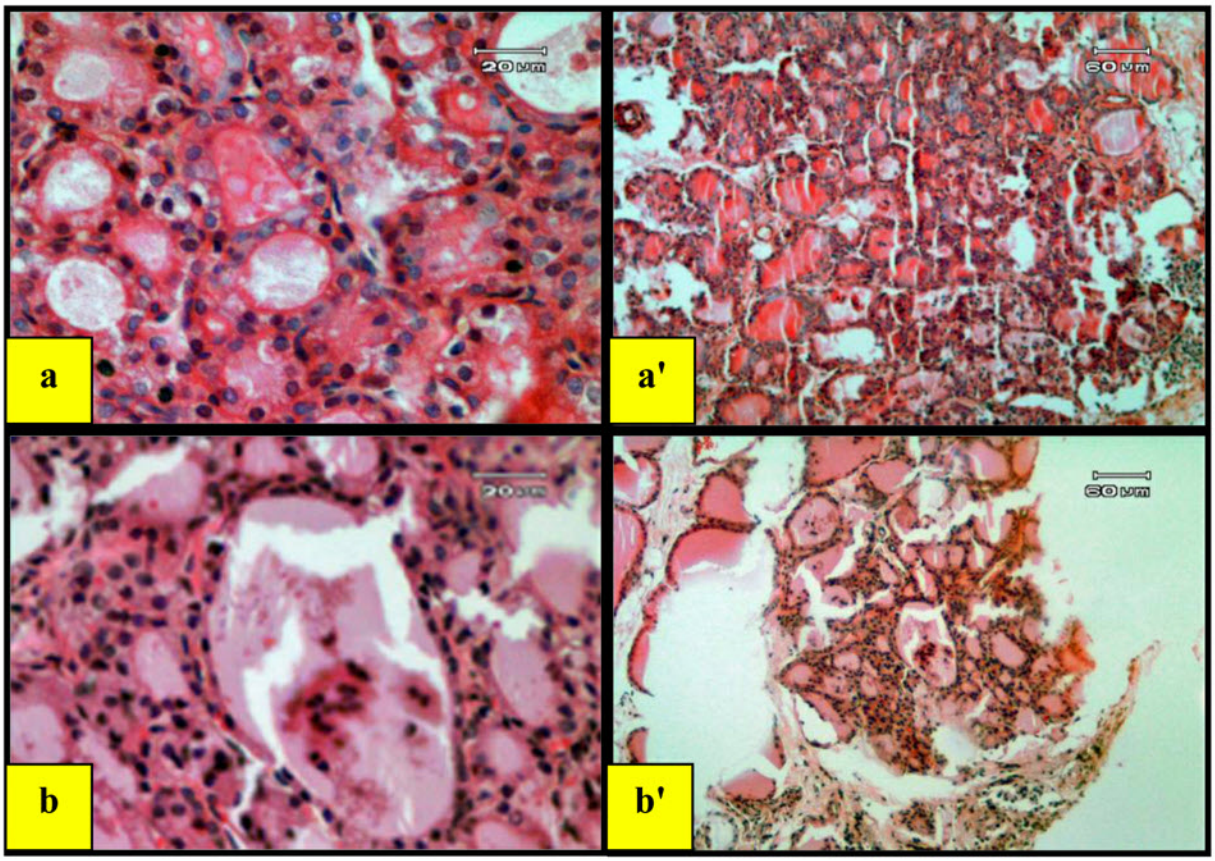

Figure 2 *(a, a') Cuboidal shape of follicular epithelium of control animals; (b, b') cylindrical and cylinderocuboidal epithelium of DMSO treated animals*

Table 2 Thyroid body indices calculated on the basis of final body weights of animals

	Thyroid Body Index (mg/100g)	
Experiment	**Control**	**DMSO Treated**
I	5.43 ± 0.41	5.91 ± 0.63
II	5.21 ± 0.51	6.07 ± 0.69
III	5.41 ± 0.51	5.91 ± 0.67
IV	6.11 ± 0.69	8.16 ± 0.48

The thyroid body indices (TBIs) of the DMSO treated animals was also found to be higher than TBIs of control animals. TBIs were calculated on the basis of final body weights of animals and may be defined as the weight of clean thyroid tissues (mg) per 100g of final body weight. High values of TBIs of DMSO treated animals not only result from the antithyroid effect of DMSO but are also additional indicative of an overactive gland. Moreover, antithyroid drugs are reported to act either through complexation with iodine or by inhibiting thyroperoxidase enzyme. We also noted complex formation between DMSO and iodine, which may be a cause of its antithyroid effects.

Conclusion

DMSO demonstrated moderate antithyroid activity in rats. Its efficacy as alternate drug for non severe hyperthyroid cases should be evaluated.

References

1. Brayton CF. Dimethyl sulfoxide (DMSO): a review. The Cornell Veterinarian1986; 76: 61-90.

2. Jacob SW, Herschler R. Pharmacology of DMSO. Cryobiology 1986; 23:14-27.

3. Jacob SW, Wood DC, Dimethyl sulfoxide (DMSO) toxicology, pharmacology, and clinical experience. Am J Surg 2004; 114:414-426.

4. Kolb KH, Jaenicke G, Kramer M, Schulze PE. Absorption, distribution, and elimination of labeled dimethyl sulfoxide in man and animals. Ann NY Acad Sci 1967;141:85-95.

5. Hammerman DL, Ritterman DP. Dimethyl sulfoxide: Influence upon frog tadpole metamorphosis. 1969; 54: 223-228.

6. Fatima I, Munawar MA, Khan MA, Asmatullah, Khalil M. Antithyroid activity of 6-chloropurine. J Braz Chem Soc 2010; 21: 1699-1703.

7. Fatima I, Munawar MA, and Tasneem A, Synthesis and antithyroid activity of some 8-substituted Purine derivatives. J mex chem Soc 2010; 54: 227-332.

 2221-0288(201201/01)1:1<33:TREODS>2.0.TX;2-M