

Effect of oral ingestion of an extract of the herb *Uncaria tomentosa* on the biodistribution of sodium pertechnetate in rats

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Abstract

The aim of the present study was to determine the effect of the oral ingestion of an extract of the herb *Uncaria tomentosa* (cat's claw) on the biodistribution of the radiobiocomplex sodium pertechnetate ($\text{Na}^{99\text{m}}\text{TcO}_4$) in rats. The animals (male Wistar rats, 2 months old, 180-220 g), were treated (1 mL) with an *U. tomentosa* extract (32 mg/mL, N = 5) or 0.9% NaCl solution (control, N = 5) for 7 days. After this period, $\text{Na}^{99\text{m}}\text{TcO}_4$ (3.7 MBq, 0.3 mL) was injected through the ocular plexus and after 10 min the rats were killed, the organs isolated and counted in a well-gamma counter. A significant ($P < 0.05$) alteration in $\text{Na}^{99\text{m}}\text{TcO}_4$ uptake i) from 0.57 ± 0.008 to 0.39 ± 0.06 %ATI/organ ($P < 0.05$) and from 0.57 ± 0.17 to 0.39 ± 0.14 %ATI/g ($P < 0.05$) was observed in the heart, ii) from 0.07 ± 0.02 to 0.19 ± 0.07 %ATI/g in the pancreas, and iii) from 0.07 ± 0.01 to 0.18 ± 0.07 %ATI/g ($P < 0.05$) in muscle after treatment with this extract. Although these results were obtained with animals, caution is advisable in the interpretation of the nuclear medicine examination when the patient is using this herb. This finding is probably an example of drug interaction with a radiopharmaceutical, a fact that could lead to misdiagnosis of the examination in clinical practice with unexpected consequences for the patient.

Key words

- *Uncaria tomentosa*
- Biodistribution
- Sodium pertechnetate
- Radiobiocomplex

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Research supported by CAPES,
FAPERJ, CNPq, UERJ, and UFF.

Received February 16, 2006

Accepted October 24, 2006

Uncaria tomentosa (cat's claw) is a medicinal herb that has been used by the indigenous people of Peru for over 2000 years. Explorers of the 1800's noticed healthy, robust natives who seemed to be disease and cancer free. They took note of a tea the natives were constantly drinking which was obtained from the bark of this woody vine (1).

U. tomentosa was brought to Europe and in the 1990's it became a complementary treatment for AIDS and cancer (1,2). It is a potent plant with 29 described chemical constituents including 17 different alkaloids with actions considered to be anti-depressant, anti-oxidant, anti-inflammatory, anti-mutagenic, anti-hypertensive, anti-viral, anti-ulcerous,

cytoprotective, and immunomodulating (2,3).

Despite the beneficial effects reported by users, the indiscriminate use of this and other plants and infusions without medical advice/criteria can be dangerous (4,5). Several cases of toxic effects of medicinal plants have been reported; however, the toxicity, drug interaction and side effects of these products are not completely known (4,5).

Radiopharmaceuticals (radiobiocomplexes) (6) are radioactive tracers employed in nuclear medicine for the study of several morphological and physiological conditions, such as blood flow and absorption, biodistribution, and metabolism in target and non-target organs (7).

Many natural and synthetic products have been reported to affect the biodistribution of different radiobiocomplexes (6-9). The incorporation of a radionuclide into a drug formulation permits the determination of the biodistribution kinetics and the release sites of the latter (10,11). Technetium-99m (Tc-

99m) has been widely used in nuclear medicine due to its optimal half-life (6.0 h) and energy characteristics, providing images with high efficiency with the administration of low doses to the patient (10,11). Radiobiocomplexes such as sodium pertechnetate ($\text{Na}^{99\text{m}}\text{TcO}_4$) are tracers widely employed in scintigraphic studies (single-photon emission computed tomography - SPECT) mainly of the thyroid but also of the brain and stomach (10,11).

Since human beings that are using *U. tomentosa* may need a nuclear medicine procedure, the aim of the present study was to evaluate the effect of *U. tomentosa* on the biodistribution of the radiobiocomplex $\text{Na}^{99\text{m}}\text{TcO}_4$ in an experimental model using Wistar rats.

Aqueous preparations of a commercial *U. tomentosa* extract (Cats Claw, Herbarium Foundation for Health and Research, Curitiba, PR, Brazil, Lot No. 830283) were obtained using 0.9% NaCl. To obtain the preparation considered to be 100%, 320 mg lyophilized leaves (dried) of *Uncaria* was placed in a vial with 10 mL saline solution (0.9% NaCl) at room temperature. This preparation was centrifuged in a clinical centrifuge (1500 rpm, 5 min) and the supernatant, 32 mg/mL, was considered to be 100%.

Two-month-old male Wistar rats (180-220 g) were obtained from Laboratório de Radiofarmácia Experimental (Departamento de Biofísica e Biometria, Universidade do Estado do Rio de Janeiro, Rio de Janeiro, RJ, Brazil) and maintained in a room under controlled conditions ($22 \pm 5^\circ\text{C}$, 12-h light/dark cycle), with free access to water and a normal diet. Experiments were conducted in accordance with the Department Committee of Animal Care and with the institutional guidelines, in compliance with national laws and Guidelines for the Use of Animals in Biomedical Research (12).

The *U. tomentosa* preparation (32 mg/mL) was administered (1 mL) to the animals (N = 5) by gavage for 7 days. The control group

Table 1. Effect of an orally administered aqueous extract of *Uncaria tomentosa* on the biodistribution of the $\text{Na}^{99\text{m}}\text{TcO}_4$ radiobiocomplex reported as %ATI/organ and %ATI/g of tissue.

Organ	%ATI/organ		%ATI/g tissue	
	Control	Treated	Control	Treated
Brain	0.13 ± 0.07	0.13 ± 0.07	0.09 ± 0.05	0.08 ± 0.03
Liver	0.26 ± 0.36	0.71 ± 0.51	2.86 ± 0.65	2.23 ± 0.47
Duodenum	0.21 ± 0.06	0.31 ± 0.12	0.61 ± 0.33	0.65 ± 0.01
Heart	0.57 ± 0.01	0.39 ± 0.06*	0.57 ± 0.17	0.39 ± 0.14*
Kidney	0.15 ± 0.16	0.14 ± 0.06	0.54 ± 0.41	0.75 ± 0.06
Spleen	0.12 ± 0.03	0.11 ± 0.07	0.71 ± 0.60	0.50 ± 0.20
Lung	0.33 ± 0.17	0.42 ± 0.10	2.07 ± 0.94	1.64 ± 0.41
Stomach	0.50 ± 0.13	0.37 ± 0.18	7.65 ± 1.16	7.70 ± 0.94
Pancreas	0.03 ± 0.01	0.08 ± 0.07	0.07 ± 0.02	0.19 ± 0.07*
Blood	1.43 ± 0.07	1.32 ± 0.11	1.43 ± 0.07	1.32 ± 0.11
Bone	0.08 ± 0.05	0.09 ± 0.05	0.30 ± 0.08	0.27 ± 0.05
Muscle	0.02 ± 0.01	0.10 ± 0.02	0.07 ± 0.01	0.18 ± 0.07*
Thyroid	0.78 ± 0.16	0.54 ± 0.21	4.97 ± 0.85	4.24 ± 2.27
Testis	0.25 ± 0.02	0.16 ± 0.14	0.26 ± 0.10	0.11 ± 0.10

Data are reported as mean ± SD for 5 animals in each group. After 7 days of treatment with an *Uncaria tomentosa* extract by gavage (control, 32 mg/mL), male Wistar rats received 0.3 mL $\text{Na}^{99\text{m}}\text{TcO}_4$ by the intravenous route. The animals were sacrificed, the organs isolated and %ATI/organ and %ATI/g tissue determined.

*P < 0.05 compared to the respective control (ANOVA).

received 0.9% NaCl (N = 5). $\text{Na}^{99\text{m}}\text{TcO}_4$ (0.3 mL, 3.7 MBq; Instituto de Pesquisas Energéticas e Nucleares, Comissão Nacional de Energia Nuclear, São Paulo, SP, Brazil) was injected through the ocular plexus and the animals were sacrificed 10 min later.

The organs (brain, liver, duodenum, heart, kidney, lung, spleen, stomach, pancreas, testis, blood, bone, muscle, and thyroid) were isolated and weighed on a clinical scale and radioactivity was counted in a well counter (Automatic, Gamma Counter, Packard, Meriden, CT, USA). The percentages of radioactivity per organ (%ATI/organ) and per gram (%ATI/g) of each organ were calculated. Data were analyzed statistically by ANOVA followed by the *t*-test, with the level of significance set at $P < 0.05$.

Table 1 shows the %ATI/organ of the radiobiocomplex $\text{Na}^{99\text{m}}\text{TcO}_4$ in the animals treated with *U. tomentosa* and in the control group. A significant ($P < 0.05$) decrease in the uptake of this radiobiocomplex from 0.57 ± 0.008 (control) to 0.39 ± 0.06 %ATI/organ was observed in the heart ($P = 0.0009$). Table 1 also shows the %ATI/g tissue of $\text{Na}^{99\text{m}}\text{TcO}_4$ for the animals treated with *U. tomentosa* and for the control group. A significant ($P < 0.05$) increase in $\text{Na}^{99\text{m}}\text{TcO}_4$ uptake from 0.07 ± 0.02 (control) to 0.19 ± 0.07 %ATI/g in the pancreas ($P = 0.018$) and from 0.07 ± 0.01 (control) to 0.18 ± 0.07 %ATI/g in muscle ($P = 0.03$) was observed after treatment with the extract. A significant ($P < 0.05$) decrease in the uptake of this radiobiocomplex from 0.57 ± 0.17 (control) to 0.39 ± 0.14 %ATI/g was also observed in the heart ($P < 0.05$).

The results obtained suggest that the *U. tomentosa* extract can act on the biodistribution of $\text{Na}^{99\text{m}}\text{TcO}_4$ in specific organs. Diré et al. (12) reported that the *in vitro* labeling of blood constituents with Tc-99m (another radiobiocomplex prepared) and the morphometry of red blood cells were unchanged in rats treated *in vivo* with *U. tomentosa*. The results obtained by these investigators with *U. tomentosa* in another experimental protocol and the

findings of the present study indicate that the herb-radiobiocomplex interaction depends on the experimental conditions employed and on the radiobiocomplex studied.

Some studies are available about the effects of several natural and synthetic substances on the biodistribution of the $\text{Na}^{99\text{m}}\text{TcO}_4$ radiobiocomplex. Moreno et al. (6) reported that *Ginkgo biloba* extract altered the uptake of $\text{Na}^{99\text{m}}\text{TcO}_4$ in several organs. Diré et al. (8) demonstrated that natural products such as chayotte extracts can also induce changes in the biodistribution of $\text{Na}^{99\text{m}}\text{TcO}_4$. Jankovic and Djokic (9) reported the alteration of the organ uptake of several radiobiocomplexes labeled with Tc-99m induced by the administration of the cytotoxic drugs methotrexate sodium and cyclophosphamide using this same experimental model.

When the drug interaction with radiobiocomplexes is unknown, the examination is not recommended, since the consequences of the procedure are the possibility of misdiagnosis and/or repetition of the examination, with an increase in the radiation dose administered to the patient (7,13). When the drug interaction with radiobiocomplexes is known, whether desirable or undesirable, the natural consequence is a correct diagnosis (7).

Since in the present study the treatment with *Uncaria* decreased the uptake of $\text{Na}^{99\text{m}}\text{TcO}_4$ by heart, pancreas and muscle, these findings could be considered to be an example of herb interaction with radiobiocomplexes. The knowledge about this phenomenon represents important clinical information for the best therapeutic decision and correct diagnosis.

Acknowledgments

We thank the Herbarium Foundation for Health and Research, Curitiba, PR, Brazil, for the donation of the *Uncaria tomentosa* extract.

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