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Biodistribution Study of the Radiopharmaceutical Sodium Pertechnetate in *Wistar* Rats Treated with Rutin

[1]Luciana C. Bernardo, [1]Ana E.O. Santos, [1]Danielle C. Mendes, [1]Carolina K. Ribeiro,
[1]Maria L. Gomes, [1]Gláucio Diré, [1]Leandro M. Jesus, [1]Paulo R.C. Abreu,
[1]Rafael Pereira, [1]Jacques N.G. Frydman, [2]Roberto S. Moura and [1,3]Mario Bernardo-Filho
[1]Biophysics and Biometry Department [2]Pharmacology and Psicobiology Department,
Roberto Alcantara Gomes Biology Institute,
Universidade do Estado do Rio de Janeiro, Av. 28 de setembro, 87, 20551-030, Rio de Janeiro, RJ, Brasil
[3]Instituto Nacional do Câncer, Praça da Cruz Vermelha, 23, 20230-130, Rio de Janeiro, RJ, Brasil

Abstract: The interest of scientific community in the research of biological effects of medicinal plants is increasing. Among the different substances isolated from natural products, stands out flavonoids. Rutin is a flavonoid used in conventional and traditional medicine. In nuclear medicine, radiopharmaceuticals present an expected biodistribution and uptake in determined target organs. However, studies show that biodistribution can be altered by the use of natural or synthetic substances. In this study, we evaluated the biodistribution of the radiopharmaceutical sodium pertechnetate ($^{99m}TcO_4Na$) in *Wistar* rats treated with rutin. Male *Wistar* rats were divided in two groups: treated with rutin (n=5) and treated with NaCl 0.9% (n=5). $^{99m}TcO_4Na$ was administered and the radioactivity percentage per gram of each organ was determined (%ATI.g^{-1}). The results show that rutin interfered on the uptake of $^{99m}TcO_4Na$ in liver (P=0.0026), when compared with group 2. The results can be explained by the pharmacological effects of this flavonoid like hepatoprotective actions.

Key words: Rutin, biodistribution, sodium pertechnetate, flavonoid

INTRODUCTION

The use of natural products is growing in the world. Due to this fact, the interest of the scientific community in studying the biological actions of medicinal plants is increasing[1]. Many substances can be isolated from medicinal plants, each one has its own characteristics, like chemical structures and pharmacological effects. Flavonoid is one of these substances isolated from medicinal plants which presents therapeutic importance. They are absorbed by digestive via and present low toxicity. This substance presents many biological effects, like anti-inflammatory and antispasmodic[2]. Rutin is a well-known flavonoid, which has been suggested many pharmacological activities, including myocardial protection[3], vasodilator[3], triacylglycerol levels reducer[4], angioprotector[5] and antioxidant agent[6,7].

In nuclear medicine, radioactive tracers, known as radiopharmaceuticals, are employed in blood flow, metabolism, morphology of an organ[8] and to evaluate the drug formulation and drug delivery systems[9]. Radiopharmaceuticals are designed to have specific biodistribution and uptake in determined targets and/or elimination patterns when administered to normal subjects[8]. Technetium-99m (^{99m}Tc) has been the most utilized radionuclide in nuclear medicine procedures and it is also used in basic research. The wide use in nuclear medicine is due to its optimal physical characteristics (half-life of 6 h, gamma rays energy of 140 keV and minimal dose to the patients), convenient availability from $^{99}Mo/^{99m}Tc$ generator and negligible environmental impact[10]. The radiopharmaceutical sodium pertechnetate ($^{99m}TcO_4Na$) is the form of ^{99m}Tc eluted from the $^{99}Mo/^{99m}Tc$ generator and it is used in nuclear medicine to obtain images from thyroid, gastric mucosa, salivary glands, choroids plexus of the brain[11]. An unexpected patterns of radiopharmaceuticals distribution provoke a flurry of inquires regarding the quality of administered agent. But, the alterations in biodistribution may be related to drug interaction with radiopharmaceuticals[12]. In literature, many authors described that drugs (natural or synthetics) can alter the bioavailbility of radiopharmaceuticals, like

Corresponding Author: Luciana C. Bernardo, Universidade do Estado do Rio de Janeiro, Roberto Alcantara Gomes Biology Institute, Biophysic and Biometry Department, Mario Bernardo-Filho, Av. 28 de setembro, 87, Zip code: 20551-030, Phone: 55 21 22543532, Fax: 55 21 25876432
E-mail: bernardo@uerj.br / lucianabernardo@click21.com.br

Gomes *et al.*[12] that reported that mitomycin-C alter the biodistribuition of ^{99m}Tc labeled sodium pyrophospate (^{99m}Tc-PYP)[13]. In this study we evaluated the biodistribution of the radiopharmaceutical $^{99m}TcO_4Na$ in *Wistar* rats treated with rutin.

MATERIALS AND METHODS

Ten male *Wistar* rats were used to perform the experiment. The animals were divided in two groups: treated (n=5) and control (n=5). Rutin (Sigma, USA) solution (20 mg.kg^{-1}) was administered for treated group during 8 days and saline solution (NaCl 0.9%) for control group in the last day. In this day, was injected by ocular plexus 0,3 mL of $^{99m}TcO_4Na$ (3.7 MBq). After 10 min the animals were sacrificed and the organs were removed, weighted and radioactivity of each organ was obtained in a well counter (Clinigamma, gamma counter, LKB, Wallac, Finland). The radioactivity percentage per gram of each organ was determined (%ATI.g^{-1}). The statistical analyses were performed with Student's *t*- test (P<0.05).

RESULTS AND DISCUSSION

The results show that rutin interfered in the uptake of $^{99m}TcO_4Na$ in liver (P=0.0026). In control group the %ATI.g^{-1} was 1.08±0.19, while in treated group was 1.90±0.38 (Table 1). In literature is related that many drugs were capably to modify the bioavailbility of radiopharmaceuticals[12]. Gomes *et al.*[13] showed that mitomycin-C due to its toxicity alter the biodistribution of ^{99m}Tc-PYP. Mattos *et al.*[14] observed that vincristine modify the bioavailability of ^{99m}Tc-dimercaptosuccinic acid (^{99m}Tc-DMSA) and ^{99m}Tc-diethylenetriamine-pentaacetic acid (^{99m}Tc-DTPA) probably due to the toxic and immunosuppressive effects of this drug. Diré *et al.*[15] related that *Sechium edule* was capable to alter the uptake of $^{99m}TcO_4Na$ in some organs in *Wistar* rats. This alteration is associated to the generation of active metabolites with lesive properties in specific biological system[15].

Table 1: Effect of rutin on the biodistribution of $Na^{99m}TcO_4$ activity per gram in organs isolated from *Wistar* rats

Organs	Control (%ATI.g^{-1})	Treated (%ATI.g^{-1})
Stomach	4.67±1.41	5.01±3.01
Thyroid	3.81±2.34	8.51±7.10
Blood	1.02±0.19	2.30±0.93
Pancreas	0.15±0.08	0.59±0.62
Duodenum	1.32±0.66	1.70±1.04
Spleen	0.36±0.21	0.83±0.17
Testis	0.19±0.07	0.33±0.12
Kidney	0.73±0.20	1.56±0.37
Heart	0.37±0.09	0.87±0.14
Lung	1.00±0.24	1.80±0.31
Bone	0.28±0.08	0.57±0.11
Muscle	0.14±0.04	0.31±0.05
Liver	1.08±0.19	1.90±0.38*
Brain	0.06±0.02	0.09±0.03

The percentages of activity per gram (%ATI.g^{-1}) were compared with control and treated groups. Statistical analyses were performed (Student's *t*-test, P<0.05). The values are presented as means ± standard deviation.
*P<0.05, when compared with control group

In conclusion, rutin increased the uptake of $^{99m}TcO_4Na$ in liver, that can be explained by the pharmacological effects of this flavonoid, like hepatoprotective actions[3].

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