Quantitative and qualitative examination of kidney scintigraphy of normal White New Zealand rabbit after administration of saffron

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Abstract

Scintigraphy is a diagnostic and therapeutic technique in nuclear medicine. Its first applications in the 1970s involved imaging organs such as the brain, liver, spleen, etc. By the 1980s, radiopharmaceuticals were employed for diagnosing cardiac conditions. Today, nuclear medicine is recognized for its high accuracy in the diagnosis, prevention, and treatment of various diseases. Key advantages of nuclear medicine include rapid disease diagnosis, assessment of disorder extent, real-time evaluation of disease progression, and precise reporting on surgical outcomes for specific patients. Renal scintigraphy, also known as kidney scanning or imaging, is a valuable technique for assessing kidney function. This method utilizes radioisotopes to examine both the function and anatomy of the kidneys. Other methods for assessing kidney morphology include radiology, ultrasonography, MRI, and computed tomography; however, scintigraphy offers the unique advantage of physiological imaging. Given the previously demonstrated blood flow-enhancing effects of saffron, this study aims to quantitatively and qualitatively analyze the kidneys of four healthy New Zealand White rabbits using the radiopharmaceutical 99mTc-DTPA. We will investigate and compare overall and individual GFR, peak times, and other parameters before and after the administration of saffron extract. Results indicate an increase in GFR and a reduction in peak time following saffron extract use.

Keywords: Kidney, New Zealand White rabbit, Saffron, Scintigraphy.

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Introduction

Several diagnostic methods are available for assessing kidney function, including ultrasonography, computed tomography (CT), magnetic resonance imaging (MRI), and renal scintigraphy. Nuclear medicine techniques, or scintigraphy, can be categorized into laboratory and in vivo assessments (either static or dynamic) for evaluating renal function (Caglar *et al*., 2008, 2008; Berger *et al*., 2017).

Nuclear medicine has been used for kidney function evaluation since the early 1950s, providing a practical tool for clinicians (James and Harvey, 2006). Scintigraphy involves the use of radioactive substances containing labeled particles, typically gamma-ray emitting isotopes with a short half-life, which possess suitable chemical properties for effective labeling and cost-efficiency (Balogh *et al*., 1999).

Dynamic imaging is often required for physiological information regarding the kidneys; however, static imaging may suffice for certain applications. Individual renal blood flow can be measured through dynamic gamma camera imaging, while glomerular filtration rate (GFR) is commonly assessed using 99mTc-DTPA (Balogh *et al*., 1999; Caglar *et al*., 2008).

The radioisotope 99mTc is favored in scintigraphy due to its lower radiation exposure for patients and its ability to label various chemical compounds (Kibar *et al*., 2003). This isotope's nearly complete glomerular filtration further supports its use in kidney studies (Kibar *et al*., 2003; Caglar *et al*., 2008).

Scintigraphy can illustrate the distribution of various substances within a living organism, quantifying this distribution and distinguishing between normal (physiological) and abnormal (pathological) tissue states. Consequently, it serves as a non-invasive, sensitive, and specific method to assist clinicians in accurate diagnosis (Caglar *et al*., 2008; Berger *et al*., 2017). This technique enables the evaluation of renal blood flow and differentiation between renal parenchyma and the urinary collecting system. Numerous kidney diseases, such as hydronephrosis, nephrolithiasis, aplasia, renal hypoplasia, asymmetry, ureteral dilation, and urinary obstruction, can be effectively diagnosed using this method. Scintigraphy facilitates the assessment of both glomerular and tubular filtration rates, which cannot be accurately obtained through ultrasonography or radiography (Caglar *et al*., 2008).

Saffron, composed of crocin, crocetin, and picrocrocin, has demonstrated antidepressant, anticonvulsant, analgesic, anticancer, and various therapeutic effects on multiple body systems, including cardiovascular, immune, respiratory, urogenital, and central nervous systems (Derakhshanfar *et al*., 2008; Mahmoudzadeh *et al*., 2017; Karimi *et al*., 2022). A study specifically investigating crocin’s effects on aged mice revealed its ability to reduce oxidative stress and inflammation (Derakhshanfar *et al*., 2008). Dakhshanfar *et al*. (2008)

examined saffron's effects on the cardiovascular system, concluding that this extract positively impacts cardiovascular health and enhances overall blood flow (Derakhshanfar *et al*., 2008).

Research conducted in 2022 demonstrated that saffron reduces blood urea nitrogen (BUN) levels, indicating beneficial effects on kidney function (Karimi *et al*., 2022). Furthermore, a 2017 study by Najafi *et al*. showed that saffron extract mitigates kidney disorders affecting blood flow (ischemia/reperfusion), emphasizing its positive impact on kidney health (Mahmoudzadeh *et al*., 2017).

The objective of this study is to investigate the effects of saffron extract on kidney parameters related to GFR, time to peak activity, and peak activity percentage before and after administration of the extract.

Materials and methods

Samples: Four male adult New Zealand White rabbits, approximately 5.5 kg (±1.2 kg) and 8 months old, were obtained from the Kerman Medical Sciences Research Center.

Preparation of Saffron Extract: Five grams of saffron were steeped in 300 cc of boiling water in a water bath at 70°C. The mixture was filtered twice through a Buchner funnel and subsequently dried in a freeze dryer to obtain a fine powder.

Preparation of 99mTc-DTPA Radiopharmaceutical: To prepare the radioactive technetium, a vacuum vial was placed in a designated generator chamber. Gradually, the radioactive molybdenum within the generator decayed and was eluted to convert into technetium, which was then collected in the vacuum vial. A typical dose of 99mTc-DTPA for an adult is 15 to 17 mCi; for the rabbits, a dose of 4 mCi was prepared.

Kidney Scanning: To obtain scintigraphic data, four adult male laboratory rabbits were selected, ensuring their kidney health through clinical examinations and laboratory tests, including BUN and creatinine levels. The scintigraphy was conducted in two stages: first, prior to the intraperitoneal administration of saffron, and then after.

Animals were fasted for 12 hours prior to each scan, with free access to water. The rabbits were anesthetized with 10% ketamine at a dose of 60 mg/kg and 2% xylazine at a dose of 10 mg/kg.

Dosage of Saffron Extract: The prepared powder was administered at a dose of 90 mg/kg body weight, injected intraperitoneally two hours prior to the intravenous administration of 99mTc-DTPA.

Procedure for Kidney Scanning: For scintigraphy using 99mTc-DTPA, the rabbit was positioned supinely on the scintigraphy device's table. The syringe containing the radiopharmaceutical was placed at the anatomical sites of the bladder and kidneys. Emitted radiation was recorded by a gamma camera, with the midpoint between the two kidneys centered on the monitor. Due to the small size of the subjects, the camera

was set to zoom, with zero rotation. The scanning duration was set to 30 minutes.

The injection of the radiopharmaceutical was performed using an insulin syringe into the ear vein of the animal, simultaneously with the scanning process. For the injection after saffron extract administration, this extract was given 15 minutes prior to the scan. The flow of the radiopharmaceutical from the abdominal aorta to the kidneys and its subsequent drainage into the bladder was visually recorded on the monitor as a continuous film.

The software program provided values for specific and overall GFR parameters, peak activity, and the contribution of each kidney to drainage, with data collected separately for each rabbit. The reported information was calculated both individually and as averages for the two groups. At the end of the imaging procedure, syringes containing the radiopharmaceutical were disposed of in lead-shielded containers, and the animals' conditions were monitored from behind a lead-shielded wall.

Statistical Analysis: In this study, statistical data were analyzed using SPSS software version 26. A significance level of less than 0.05 was considered statistically significant.

Results

The findings of this study indicated that the total GFR before and after saffron extract administration was 108.9±1.4 and 134.2±1.4, respectively. The individual GFR values before administration were 53.7 ± 3.7 for the left kidney and 55.2±4.5 for the right kidney, changing to 68.3±3.7 and 65.9±4.5, respectively, after treatment. Both indicators demonstrated statistically significant differences (p<0.05). Notably, the functional division of both kidney groups exceeded 40%, indicating kidney health before and after saffron extract administration. Clinical findings from scintigraphy in both the control and extract groups indicated complete kidney health. Additional data can be found in Figures 1 and 2, and Table 1.

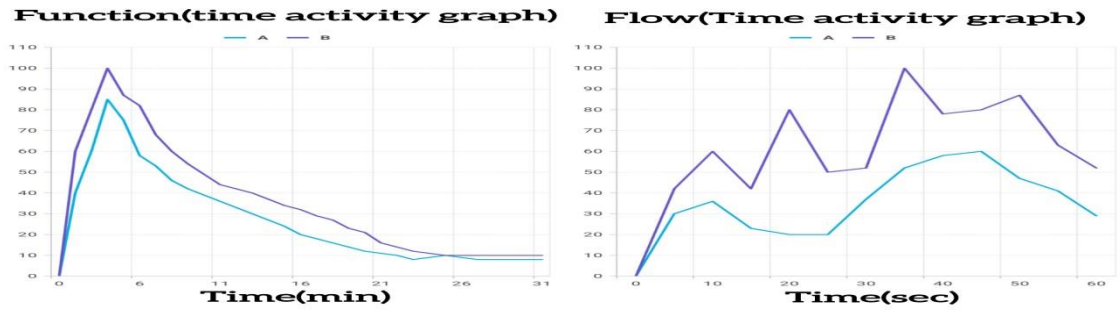

Figure 1: Dynamic renal scintigraphy prior to the administration of saffron was performed using the radiopharmaceutical 99mTc-DTPA in both flow and functional phases.

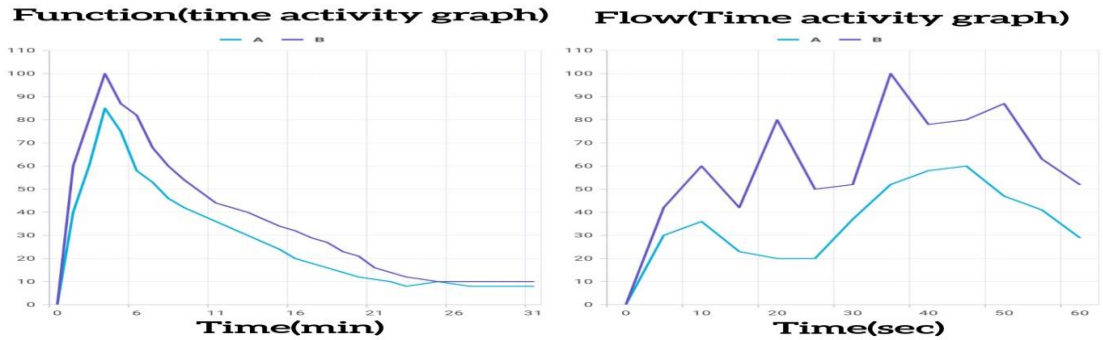

Figure 2: Dynamic renal scintigraphy following the administration of saffron was performed using the radiopharmaceutical 99mTc-DTPA in both flow and functional phases.

Table 1: The measured parameters of the dynamic scan of kidneys of rabbits before and after the administration of saffron

Parameters	Average Parameters and before the administration of saffron	Average Parameters and after the administration of saffron
Total GFR	108.9+-1.4	134.2+-1.4
Individual GFR	L:53.7+-3.7 R:55.2+-4.5	L:68.3+-3.7 R:65.9+-4.5
Time to peak activity(min)	L:3.3+-0.5 R:4.1+-0.4	L:2.3+-0.3 R:2.9+-0.6
Emptying half time(min)	L:9.1+-0.5 R;10.6+-0.6	L:6.4+-0.6 R:6.7+-0.7

Discussion

The kidneys are essential organs responsible for regulating osmotic pressure and maintaining homeostasis (McDonald and Grosell, 2005). Scintigraphy can assess physiological functions of various organs, including the kidneys, allowing for the measurement of both tubular and glomerular filtration rates (Kibar *et al*., 2003). This technique is highly accurate and non-invasive, making it an ideal choice for examining different tissues (Kibar *et al*., 2003; Benjamens *et al*., 2018).

In 2008, scintigraphy was utilized to investigate the potential presence of hydronephrosis and obstruction at the ureter-pelvic junction. Results confirmed that scintigraphy is an accurate method for assessing kidney disorders (Chung *et al*., 1993; Benjamens *et al*., 2018). Frisk *et al*. (2007) found that scintigraphy can detect early kidney lesions caused by diabetes, underscoring the method's significance in kidney disorder assessments (Frisk *et al*., 2007). Kibar *et al*. (2003) concluded that static scans could identify lesions in the renal parenchyma (Kibar *et al*., 2003). Furthermore, Berger *et al*. (2017) stated that scintigraphy can evaluate renal perfusion and urology (Berger *et al*., 2017).

These studies indicate the ideal application of scintigraphy in examining dynamic changes in the kidneys due to the effects of renal drugs. In this study,

saffron extract was used, and the reasons for its selection will be discussed further.

Dakhshanfar *et al*. (2008) noted the direct effect of saffron extract on vascular blood flow and its indirect influence on the cardiovascular system (Derakhshanfar *et al*., 2008). A 2017 study reported that saffron extract reduced serum creatinine levels, suggesting increased renal activity following saffron administration (Mahmoudzadeh *et al*., 2017). Additionally, Karimi *et al*. (2022) found that saffron extract lowered BUN levels, but unlike the previous study, there was no significant change in serum creatinine after saffron injection (Karimi *et al*., 2022).

The findings of this study suggest that saffron extract enhances renal blood flow and kidney efficiency indicators while decreasing the half-life of radiopharmaceuticals, indicating improved drug clearance rates. These observations highlight the potential reinforcing, preventive, and therapeutic properties of saffron extract on kidney health.

Conclusion

This study demonstrates that saffron extract has a significantly positive effect on the kidneys of healthy rabbits. Future studies are recommended to investigate the effects of this extract on kidneys affected by diabetes or physical injuries, using scintigraphy to confirm therapeutic effects and potential preventive measures in early stages.

Ethical considerations

No human samples were used in this study, and all ethical principles regarding animal research were strictly followed.

Conflict of interest

The author declares any conflict of interest.

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Competing interests

The authors declare that there is no conflict of interest.

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