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Svitlana Marchyshyn
Department of Pharmacognosy
with Medical Botany,
Pharmaceutical Faculty, I.
Horbachevsky Ternopil State
Medical University, Ruska,
Ternopil, Ukraine

Oksana Doroshenko
Department of Pharmacognosy
with Medical Botany,
Pharmaceutical Faculty, I.
Horbachevsky Ternopil State
Medical University, Ruska,
Ternopil, Ukraine

Olga Koyro
Department of Pharmacology,
Pharmaceutical Faculty,
National University of
Pharmacy, Kharkiv, Ukraine

Sofia Nakonechna
Department of Physiology with
the Basics of Biosafety and
Bioethics, Medical Faculty, I.
Horbachevsky Ternopil State
Medical University, Ruska,
Ternopil, Ukraine

Correspondence

Svitlana Marchyshyn
Department of Pharmacognosy
with Medical Botany,
Pharmaceutical Faculty, I.
Horbachevsky Ternopil State
Medical University, Ruska,
Ternopil, Ukraine

Investigation of antioxidant and membrane stabilizing activity of plant collection with nephroprotective properties

Svitlana Marchyshyn, Oksana Doroshenko, Olga Koyro and Sofia Nakonechna

Abstract

The antioxidant and membrane stabilizing activity of plant collection, containing *Polygoni avicularis* herba, *Fragariae* herba, *Juglandis folium*, *Uvae ursi folia*, *Urticae folia*, *Elymi repensis rhizomata et radices* (25,0 for each) and *Helichrysi arenarii Flores* (20,0), has been estimated on the model of glycerol-induced acute renal failure in rats. It has been found out that the infusion (1:10) of the plant collection at a dose of 10 ml/kg suppressed lipid peroxidation processes and increased catalase activity, as well as reference drug «Chophytol» at a dose of 100 mg/kg. The original medicinal plant collection did not have the influence on the red blood cells osmotic resistance in intact animals, as well as under conditions of glycerol-induced acute renal failure.

Keywords: plant collection, infusion, antioxidant activity, nephroprotective agents, rats

1. Introduction

The actual prevalence of acute renal failure (ARF) in the world, despite the severity of this pathology, is unknown. According to a recent meta-analysis of 312 studies, involving nearly 50 million patients, the overall rate of acute renal failure and mortality due to it among hospital adult patients is 21.6% and 23.9% respectively. In recent years, the incidence of ARF has increased significantly [11, 13]. There is ample evidence that the damage caused by lipid peroxidation, plays an important role in the pathogenesis of renal failure [7, 12]. Rhabdomyolysis and intravascular hemolysis are one of the leading causes of the development of nephrotoxic acute renal failure, in the pathogenesis of which changing the antioxidant-prooxidant balance plays an important role [12]. For the purpose of correction of renal dysfunction, It is expedient to use medicines of plant origin, which, due to the multicomponent composition, can affect various links of the ARF pathogenesis.

The aim of the work is to investigate the antioxidant and membrane-stabilizing effect of the original plant collection under the conditions of myoglobinuric acute renal failure in rats.

2. Materials and methods.

According to the previous studies, we had found out that plant collection, consisting of *Polygoni avicularis* herba, *Fragariae* herba, *Juglandis folium*, *Uvae ursi folia*, *Urticae folia*, *Elymi repensis rhizomata et radices* (25,0 for each) and *Helichrysi arenarii Flores* (20,0), has nephroprotective activity under conditions of glycerol-induced ARF in mice [5]. It is expedient to study the antioxidant and membrane stabilizing action of the plant collection in order to define the possible mechanisms of nephroprotective activity [10]. The influence of plant collection infusion on the antioxidant-prooxidant balance was studied under conditions of glycerol-induced ARF. Experiments were performed on white, non-breeding female rats weighing 220-250 g, which were kept in standard conditions of the vivarium with free access to water and food. Animals were divided into 4 groups: control; model pathology (glycerol); glycerol + infusion of plant collection, 10 ml / kg; glycerol + "Chophytol", 100 mg / kg. The infusion of plant collection and "Chophytol" were administrated intragastrically to the animals for 6 days before and a day after the renal acute failure simulation. The animals of the control and model pathology groups received water in equivalent volume intragastrically. Myoglobinuric ARF was caused by intramuscular administration of 50% glycerol solution with isotonic sodium chloride solution at a dose 10 ml / kg of rats' body weight [6]. Animals of the control group received the intramuscular injection of equivalent volume of 0.9% sodium

chloride solution. The animals were decapitated under thiopental-sodium anesthesia one day after the ARF modeling, blood was collected, kidneys and liver were extracted and were determined their weight coefficients. The concentration of TBA-positive substances was determined in blood plasma (anticoagulant - heparin *in vitro*) and kidney homogenate; in the kidneys - activity of catalase and superoxide dismutase (SOD). The quantity of TBA-reactants was measured according to [9] (molar extinction coefficient of trimethine complex - $1.56 \cdot 10^5 \text{ M}^{-1} \cdot \text{cm}^{-1}$), catalase activity - according to [4] (coefficient of molar extinction of peroxide - hydrogen $2.22 \cdot 10^4 \text{ mM}^{-1} \text{ cm}^{-1}$), the activity of SOD was determined by the modified method [8]. Indicators of the prooxidant-antioxidant balance of rats with glycerol-induced ARF were calculated on 1 g of wet tissue. Membrane stabilizing activity was determined by the influence of investigated drugs on the erythrocytes osmotic resistance [1] after their course (6 days) administration for intact rats, as well as on the basis of glycerol-induced nephropathy (7th day of the experiment). The results were statistically processed using program Statistica 6.0. Student t-test was used cases of normal distribution, in case of absence - Mann Whitney U-test [2].

3. Results and Discussion

Glycerol-induced nephrotoxic ARF caused the increasing of the rats' kidney and liver weight coefficients in the model

pathology group (Table 1). There was a marked violation of the antioxidant-prooxidant balance. The quantity of TBA-positive substances increased on 34% in the liver ($p < 0.005$) and on 12% in the kidneys ($p > 0.01$) in the rats of the model pathology group in comparison with intact animals according to data Table 2. The activity of catalase and SOD decreased on 48 % ($p < 0.005$) and 60% respectively in the kidneys homogenate. Significant violations of the antioxidant-prooxidant balance in the model of pathology testify about the shift in the ratio between catalase and SOD activity in the direction of the latter (Table 3). The indicated ratio was similar to the same one in intact animals when the plant collection infusion and "Chophytol" were used.

The normalization of the kidney and liver weight coefficients was observed in that rats, who received plant collection infusion (Table 1). According to these indicators the investigated infusion significantly surpassed "Chophytol.". The quantity of TBA-reactive substances in plasma and kidneys did not differ from that in intact animals on the basis of treatment with study drugs (Table 2).

The activity of catalase increased under the influence of experimental pharmacotherapy. An increasing the activity of this enzyme in the kidneys of rats with nephrotoxic ARF in the plant collection group was statistically significant in comparison with the group of model pathology ($p < 0.05$). Significant changes of SOD activity were not recorded.

Table 1: Influence of plant collection infusion on rats' liver and kidney weight coefficients with myoglobinuric acute renal failure (n=23)

The conditions of the experiment, study drugs	Weight coefficient	
	Liver	Kidney
Control group	2,99±0,07	0,57±0,03
Model pathology (glycerol)	3,61±0,16***	0,66±0,03*
Glycerol + plant collection infusion, 10 ml / kg	3,09±0,06#^	0,60±0,03
Glycerol + «Chophytol», 100 ml / kg	3,45±0,06**	0,64±0,02

Note. Significant differences: control group - * ($p < 0,05$), ** ($p < 0,01$), *** ($p < 0,005$); model pathology group (glycerol) - # ($p < 0,05$); glycerol + "Chophytol", 100 mg / kg - ^ ($p < 0,05$); n – number of observations.

Table 2: Influence of plant collection infusion on the concentration of TBA-positive substances in rats' blood plasma and kidney homogenate with myoglobinuric acute renal failure (n=23)

The conditions of the experiment, study drugs	The concentration of TBA-positive substances	
	blood plasma, mcmol/l	kidney homogenate, nmol / g
Control group	7,11±0,24	115,5±7,7
Model pathology (glycerol)	9,54±0,52***	129,4±12,4
Glycerol + plant collection infusion, 10 ml / kg	7,32±0,63#	104,1±12,7
Glycerol + «Chophytol», 100 ml / kg	7,84±0,49#	91,7±11,1

Note. Significant differences: control group - *** ($p < 0,005$); model pathology group (glycerol) - # ($p < 0,05$); n – number of observations.

Table 3: Influence of plant collection infusion on enzymes activity of antioxidant defense system in rats with myoglobinuric acute renal failure (n=23)

The conditions of the experiment, study drugs	Enzymes activity of antioxidant defense system	
	Catalase, mmol H ₂ O ₂ /g tissue per min	Superoxide dismutase, cond. un. /g tissue per minute
Control group	2,38±0,08	9,01±1,24
Model pathology (glycerol)	1,14±0,16***	5,40±1,54
Glycerol + plant collection infusion, 10 ml / kg	1,65±0,14***#	5,45±1,12
Glycerol + «Chophytol», 100 ml / kg	1,49±0,15***	5,30±0,73

Note. Significant differences: the control group - *** ($p < 0,005$); model pathology group (glycerol) - # ($p < 0,05$); n – number of observations, cond. un. – conditional units.

Taking into account the above, it can be assumed that the ability to normalize the antioxidant-prooxidant balance due to the peculiarities of the phytochemical composition is one of the mechanisms of nephroprotective action of plant collection

infusion [3]. Nephroprotective effect of biologically active substances on the studied models can be caused not only antioxidant, but also membranoprotective activity, which are closely interrelated [14]. Therefore, it was important to

determine the effect of plant collection infusion on the osmotic resistance of red blood cells. Measurements were performed according to the method [1] after the course (6 days) of the administration of the drugs, as well as on 1st day after the reproduction of glycerol-induced nephropathy. As can be seen from the data in Table 4, either plant collection infusion or "Chophytol" did not have a significant

effect on the osmotic resistance of erythrocytes in intact rats and in animals with myoglobinuric ARF. The introduction of glycerol did not significantly affect the osmotic resistance of red blood cells. It is likely that its effect on cells in various types of stress is determined by the ability to change the physical and chemical characteristics of cells, which directly determine their sensitivity to the action of stress factors.

Table 4: Influence of plant collection infusion and «Chophytol» on the osmotic resistance of erythrocytes in intact rats and under the conditions of myoglobinuric acute renal failure (n=23)

The conditions of the experiment, study drugs	Degree of hemolysis, %				
	0,6% NaCl	0,5% NaCl	0,4% NaCl	0,3% NaCl	Average value
<i>Intact animals</i>					
1. Control group	0,43±0,10	0,69±0,30	52,63±14,81	93,50±2,47	38,57±3,89
2. Plant collection infusion, 10 ml / kg	0,31±0,10	0,95±0,02	72,74±5,83	95,65±3,10	42,41±1,31
3. «Chophytol», 100 ml / kg	0,25±0,08	0,34±0,09	65,84±6,23	89,14±4,29	41,68±3,70
<i>Myoglobinuric acute renal failure</i>					
4. Model pathology (glycerol)	0,42±0,11	0,73±0,12	56,02±5,20	87,62±3,64	36,20±2,13
5. Glycerol + plant collection infusion, 10 ml / kg	0,47±0,06	0,79±0,12	59,07±10,14	92,17±2,18	38,12±2,88
6. Glycerol + «Chophytol», 100 ml / kg	0,84±0,18	1,22±0,19	53,99±9,26	94,30±2,21	37,59±2,23

Note. n – number of observations.

4. Conclusions

- The infusion (1:10) of the original plant collection, which contains *Polygoni avicularis herba*, *Fragariae herba*, *Juglandis folia*, *Uvae ursi folia*, *Urticae folia*, *Elymi repensis rhizomata et radices* and *Helichrysi arenarii flores*, at a dose of 10 ml / kg, has a beneficial effect on the antioxidant-prooxidant balance in rats with glycerol-induced ARF - reduces the content of TBA-reactants in blood plasma and kidneys, increases the activity of catalase in the kidneys, no inferior or exceeding the activity of «Chophytol» at a dose of 100 mg / kg.
- Inhibition of lipid peroxidation processes and activation of enzymes of antioxidant defense system may be one of the mechanisms of nephroprotective action of plant collection.
- The original plant collection does not affect the osmotic resistance of erythrocytes in intact animals and under the conditions of glycerol-induced ARF.

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