

ндується застосовувати настої з квіток і листя бузку звичайного для догляду за жирною та проблемною шкірою обличчя.

**Матеріали та методи дослідження.** Об'єктом дослідження були листя та квітки бузку звичайного сорту Фірмамент. Сировину висушували при температурі 45-55 °С та подрібнювали до розміру часток, що проходили крізь сито з діаметром отворів 2-3 мм. Визначення основних показників якості (втрата в масі при висушуванні та зола загальна) досліджуваної сировини проводили за методиками, наведеними у Державній фармакопеї України (ДФУ) 2-го видання. Вміст екстрактивних речовин визначали за методикою ДФУ 2-го видання, наведеній у монографії «Полин гіркий». В якості екстрагента використовували воду та етанол різної концентрації - 40%, 70%, 96%.

**Результати та їх обговорення.** Для листя бузку звичайного сорту Фірмамент визначені показники якості за вимогами ДФУ: втрата в масі при висушуванні становила  $8,70 \pm 0,12\%$ ; зола загальна –  $7,33 \pm 0,85\%$ ; максимальний вихід екстрактивних речовин спостерігався при використанні 40% етанолу ( $20,12 \pm 0,16\%$ ). Для квіток бузку звичайного сорту Фірмамент втрата в масі при висушуванні склала  $5,20 \pm 0,16\%$ ; зола загальна –  $3,50 \pm 0,48\%$ ; максимальний вихід екстрактивних речовин спостерігався також при використанні 40% етанолу ( $14,30 \pm 0,94\%$ ).

**Висновки.** Отриманні результати можуть бути використанні при проведенні стандартизації листя та квіток бузку звичайного сорту Фірмамент.

## INFLUENCE OF GRAPE SEED POLYPHENOLIC EXTRACTS ON THE HEPATOBILIARY SYSTEM IN LIVER PATHOLOGY

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**Introduction.** Redox reactions are involved in numerous physiological and pathological processes; moreover, cellular homeostasis depends on the interaction between oxidants and the defense system, which includes reductants and antioxidant enzymes. The prevalence of free radicals, such as reactive oxygen species and reactive nitrogen species, at a desirable level can contribute to cell growth and differentiation. However, the overproduction of free radicals is destructive, resulting in oxidative stress and contributing to various diseases, such as cardiovascular diseases, cancer, diabetes, obesity, neurodegenerative disorders, and liver diseases.

In many cases, toxic liver damage develops as a complication of drug therapy. A significant number of medications exhibit hepatotoxic effects. These include NSAIDs (Indomethacin, Paracetamol), oral antidiabetic drugs (similar Sulfonylurea, Biguanides), antituberculous drugs (Isoniazid), antibiotics (Tetracyclines, Macrolides - Erythromycin, Oleandomycin, Rifampicin), diuretics (Furosemide), indirect-duty anticoagulants (Phenylin), Phenothiazine neuroleptics. Paracetamol is widely used in prac-

tical medicine and is an effective and relatively safe antipyretic and analgesic agent, but its prolonged use can be accompanied by toxic liver damage. This led to the relevance of investigating the therapeutic effect of polyphenolic extracts of grape seed in comparison with a hepatoprotective drug called Silibor on the model of hepatitis caused by paracetamol.

The production of mitochondrial reactive oxygen species is increased, and the glutathione content is decreased in paracetamol overdose. Role of kupffer cells in paracetamol-induced liver injury: Paracetamol activates Kupffer cells, which then release numerous cytokines and signalling molecules, including nitric oxide and superoxide. Kupffer cells are important in peroxynitrite formation. On the other hand, the activated Kupffer cells release anti-inflammatory cytokines. Role of neutrophils in paracetamol-induced liver injury: Paracetamol-induced liver injury leads to the accumulation of neutrophils, which release lysosomal enzymes and generate superoxide anion radicals through the enzyme nicotinamide adenine dinucleotide phosphate oxidase. Hydrogen peroxide, which is influenced by the neutrophil-derived enzyme myeloperoxidase, generates hypochlorous acid as a potent oxidant. Role of peroxynitrite in paracetamol-induced oxidative stress: Superoxide can react with nitric oxide to form peroxynitrite, as a potent oxidant. Nitrotyrosine is formed by the reaction of tyrosine with peroxynitrite in paracetamol hepatotoxicity.

**Aim.** Drug-induced liver injury is a significant problem, so the aim of our research was to study the hepatoprotective properties of polyphenolic extracts from "Rkatsiteli" and "Caberne" grape seeds in a model of acute medical liver injury caused by the administration of paracetamol.

**Materials and methods.** Acute drug-induced hepatitis was simulated using one of the most popular antipyretic analgesics, paracetamol, known to be hepatotoxic. The experimental animals were orally administered paracetamol at a dose of 1250 mg/kg once a day for a 24-hour period. The experimental animals were divided into five groups: the intact control group; the control pathology group; animals in the third group, in which against the background of paracetamol liver damage the reference preparation Silibor was administered at a dose of 25 mg/kg; animals in the fourth and fifth experimental groups, in which against the background of paracetamol hepatitis were administered polyphenolic extracts from "Rkatsiteli" and "Caberne" grape seeds at a dose of 0.5 ml/kg. The comparison drug Silibor was administered according to the same scheme: the first two days in parallel with paracetamol, and then one more day. On the third day, the animals were removed from the experiment by decapitation. In liver tissue, the content of TBA-active products (TBA-AP), reduced glutathione (RG) and catalase activity were determined, and the activity of alanine transaminase (ALT),  $\gamma$ -glutamyl transpeptidase (GGTP), alkaline phosphatase (ALP), total protein (TP) and urea were determined in the serum of the test animals.

**Results and discussion.** The results of the experiment on hepatoprotective effect of polyphenolic extracts from grape plant under conditions of acute paracetamol hepatitis, given in Table 1, showed that administration of paracetamol in toxic doses led to a marked increase in intensity of lipid peroxidation processes. Intensity of lipid

peroxidation was manifested by the increase of the amount of TBA-AP in the liver tissue of the control group by 36.0% and the reduced level of renewed glutathione by 35.9%. At the same time, the increase in catalase activity was not statistically significant and showed little trend.

The administration of paracetamol in toxic doses resulted in severe damage to the hepatic parenchyma, which was accompanied by the formation of necrotic cells in the central and middle sections of the hepatic lobes. Increase of ALT activity in serum of experimental animals by 2.1 times indicated the development of a pronounced cytolytic syndrome. Functional abnormalities developing against the background of paracetamol damage to the liver are obviously a consequence of metabolic changes and necrotic changes that occurred in the hepatic parenchyma. Signs of cholestatic syndrome development were observed, which was manifested by significant increase of ALP and GGTP activity in serum of animals of control pathology group.

There was also disruption of biosynthetic processes, in particular protein biosynthesis in hepatocytes, as evidenced by a significant decrease in serum protein levels. At the same time there were no significant violations of detoxification (ammonia-depleting) function of the liver (the level of urea in blood serum did not change statistically), which allows to estimate the severity of hepatocellular syndrome as moderate. The severity of the pathological changes was significantly reduced by the application of grape polyphenolic extracts and the Silibor comparison. Administration of polyphenolic extracts from "Caberne" and "Rkatsiteli" grape seeds to the tested animals was accompanied by normalization of the indices characterizing the state of LPO/AOS. Thus, the content of TBA-AP in liver tissue of the experimental animals decreased by 35.7% and 31.2%, respectively, and the level of reduced glutathione normalized similarly, increasing by 59.9% and 52.3%. Although the increase of catalase activity in serum of animals in the control pathology group was not statistically significant, it was statistically lower in animals treated with the studied polyphenol complexes from grape seeds than in untreated animals, which was not observed when using the comparison drug. Although the overall effect of the comparison drug on LPO processes and the state of the antioxidant system was less pronounced, Silibor also led to normalization of the oxidative balance. The level of TBA-AP decreased by 19.3% and the content of reduced glutathione increased by 40.1% with the use of Silibor. Although the application of the studied agents resulted in normalization of the LPO/AOS indices, the signs of cytolytic syndrome persisted. Administration of polyphenol extracts from "Caberne" and "Rkatsiteli" grape seeds to experimental animals led to a decrease in ALT activity in blood serum by 25.9% and 27.2% respectively, but enzyme activity remained elevated compared with intact control. Silibor exhibited a slightly more pronounced anticytolytic effect, reducing ALT activity by 37.3%, but also did not lead to its complete normalization. A significant improvement in the functional state of the liver was observed during treatment with Silibor and polyphenol complexes from grape seeds, which proved to be a normalization of protein synthesis function and restoration of serum proteins. At the same time, a significant decrease in GGTP activity was observed. When polyphenolic extracts from

grape seeds "Caberne" and "Rkatsiteli" were applied, GGTP activity decreased by 28.7% and 28.1%, respectively. When polyphenolic extract from grape seeds "Caberne" was administered, ALP activity was completely normalized, and in animals treated with polyphenolic extract from grape seeds "Rkatsiteli", it did not differ from the parameters of animals of intact control and control pathology groups. The changes revealed suggest a reduction in the severity of the cholestatic syndrome when using the studied polyphenolic extracts from grape seeds. At the same time, administration of Silibor resulted in complete normalization of ALP and GGTP activity, indicating the superiority of the comparison drug in its effect on the development of cholestasis syndrome.

**Conclusions.** Consequently, the obtained experimental data indicate that polyphenolic extracts from "Caberne" and "Rkatsiteli" grapes seeds show high therapeutic efficacy in conditions of acute toxic liver injury by paracetamol, have a distinct effect on peroxidation syndrome development, normalizing LPO/AOS balance, syndrome and significantly improving the functional state of the liver. It is also established that the reference preparation Silibor shows in conditions of acute paracetamol hepatitis somewhat more distinct influence, in comparison with the investigated polyphenol complexes from grape seeds, on development of cytolytic and cholestatic syndrome.