Assessment of antiglycooxidant properties of nebivolol – *in vitro* study

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The purpose of the study

The aim of our study was to evaluate antiglycating and antioxidant properties of nebivolol in *in vitro* model using oxidated bovine serum albumin (BSA)

Protein oxidation

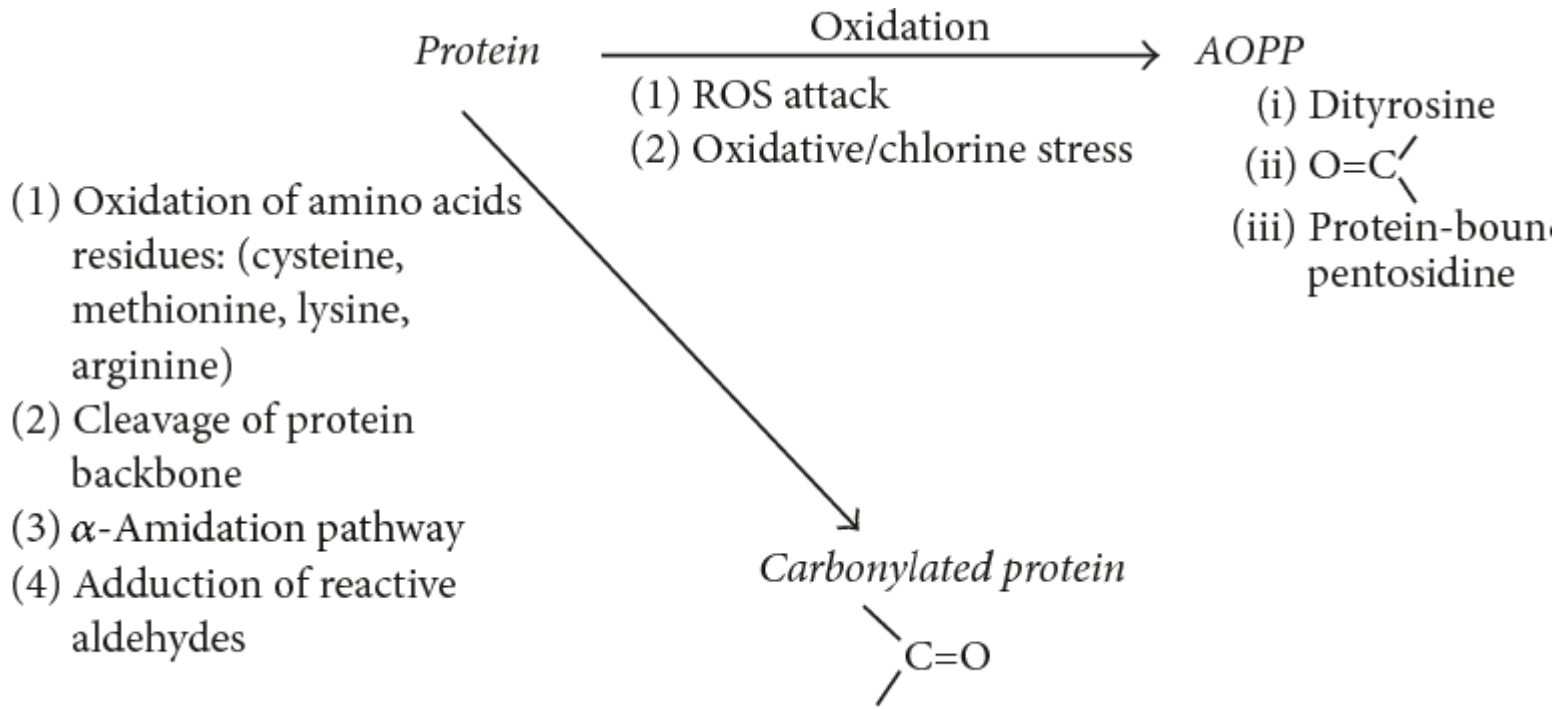

Fig. 1 – The pathways leading to formation of AOPP and carbonyl groups

Protein glycation

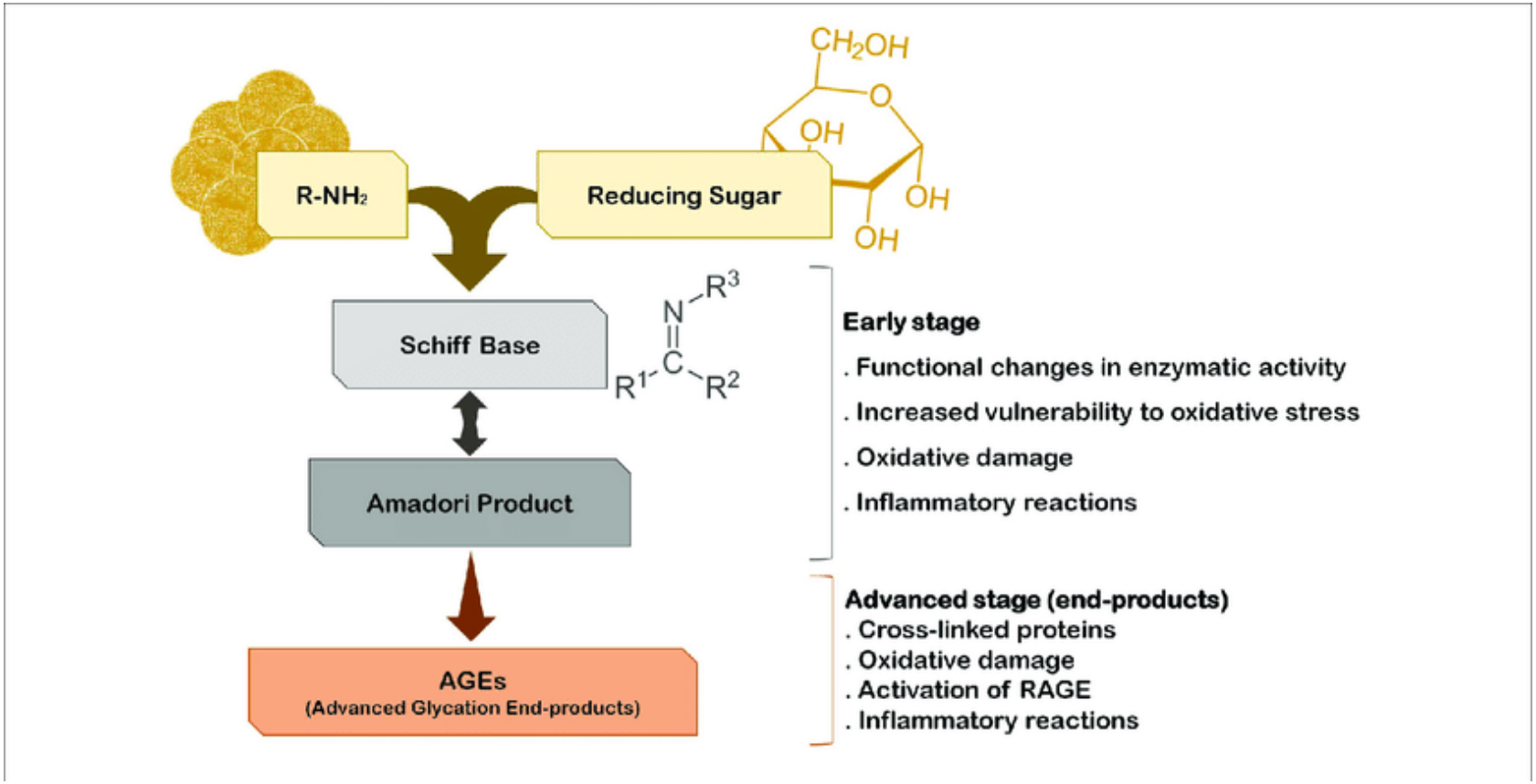

Fig. 2 – The pathway of protein glycation and AGE formation

Cardiovascular diseases

- Glycation and oxidation processes play crucial role in the development of numerous diseases

- Glycooxidation, by activation of proinflammatory factors, reducing NO bioavailibility or stimulation of remodelling and calcification of vessels, leads to atherosclerosis and – as a consequence – to hypertension, heart failure, ischemic heart diseases, etc.

Materials and methods

- 1 mM nebivolol and 0.09 mM BSA were incubated with 0.5 M glucose for six days at 37°C
- The experiment was conducted three times, each time duplicated.
- Metfomin and aminoguanidine were used of glycation inhibitors
- Captopril, Trolox, reduced glutathione, and lipoic acid were used as oxidation inhibitors

Open Access Article

A New Insight into Meloxicam: Assessment of Antioxidant and Anti-Glycating Activity in In Vitro Studies

by Cezary Pawlukianiec [1], Małgorzata Ewa Gryciuk [1], Kacper Maksymilian Mil [1], Małgorzata Żendzian-Piotrowska [2], Anna Zalewska [3] and Mateusz Maciejczyk [2,*]

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Pharmaceuticals **2020**, *13*(9), 240; https://doi.org/10.3390/ph13090240

Received: 19 August 2020 / Revised: 3 September 2020 / Accepted: 9 September 2020 / Published: 10 September 2020

(This article belongs to the Section Medicinal Chemistry)

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Abstract

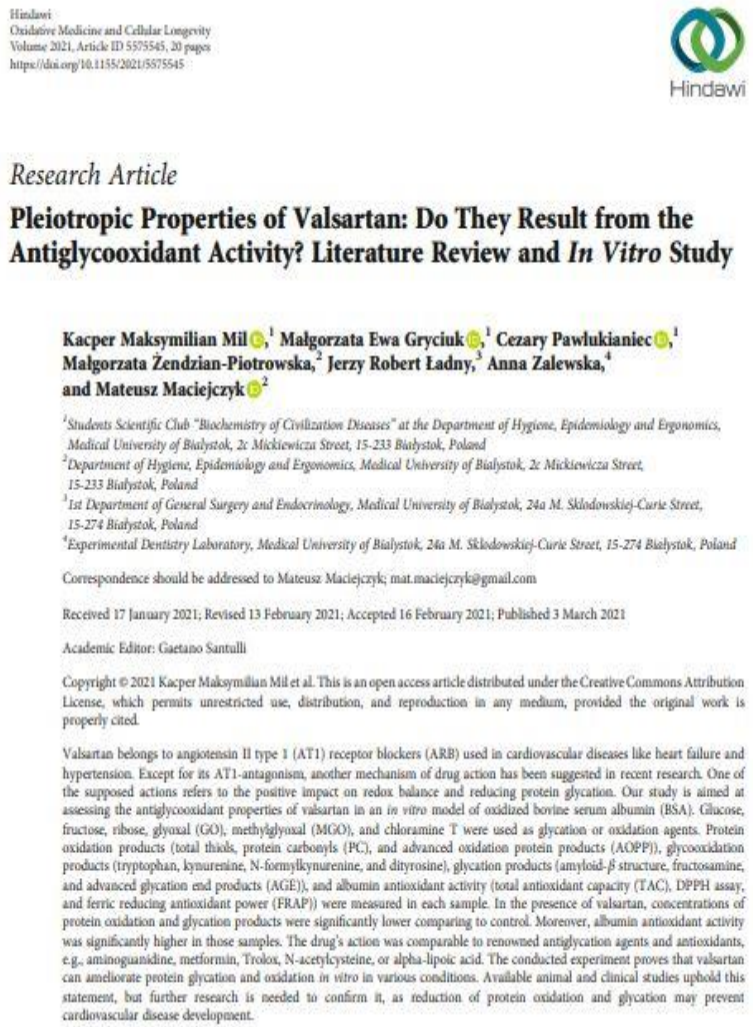
Meloxicam is a non-steroidal anti-inflammatory drug, which has a preferential inhibitory effect to cyclooxyganase-2 (COX-2). Although the drug inhibits prostaglandin synthesis, the exact mechanism of meloxicam is still unknown. This is the first study to assess the effect of meloxicam on protein glyco-oxidation as well as antioxidant activity. For this purpose, we used an in vitro model of oxidized bovine serum albumin (BSA). Glucose, fructose, ribose, glyoxal and methylglyoxal were used as glycating agents, while chloramine T was used as an oxidant. We evaluated the antioxidant properties of albumin (2,2-di-phenyl-1-picrylhydrazyl radical scavenging capacity, total antioxidant capacity and ferric reducing antioxidant power), the intensity of protein glycation (Amadori products, advanced glycation end products) and glyco-oxidation (dityrosine, kynurenine, N-formylkynurenine, tryptophan and amyloid-β) as well as the content of protein oxidation products (advanced oxidation protein products, carbonyl groups and thiol groups). We have demonstrated that meloxicam enhances the antioxidant properties of albumin and prevents the protein oxidation and glycation under the influence of various factors such as sugars, aldehydes and oxidants. Importantly, the antioxidant and anti-glycating activity is similar to that of routinely used antioxidants such as captopril, Trolox, reduced glutathione and lipoic acid as well as protein glycation inhibitors (aminoguanidine). Pleiotropic action of meloxicam may increase the effectiveness of anti-inflammatory treatment in diseases with oxidative stress etiology. View Full-Text

Keywords: meloxicam; protein glycation; protein oxidation; protein glyco-oxidation; antioxidant activity

Fig. 3 – New insight into meloxicam

Materials and methods

- The concentration of advanced oxidation protein products (AOPP) was measured by spectrophotometric detection
- The concentration of carbonyl groups (PC) and level of Amadori product were assessed colorimetrically
- The advanced glycation end products (AGE) level was analyzed spectrofluorometrically.
- The levels of dityrosine and kinurenine were detected by measuring the fluorescence emission



Hindawi
Oxidative Medicine and Cellular Longevity
Volume 2021, Article ID 5575545, 20 pages
https://doi.org/10.1155/2021/5575545

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Research Article

Pleiotropic Properties of Valsartan: Do They Result from the Antiglycooxidant Activity? Literature Review and *In Vitro* Study

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Received 17 January 2021; Revised 13 February 2021; Accepted 16 February 2021; Published 3 March 2021

Academic Editor: Gaetano Santulli

Valsartan belongs to angiotensin II type 1 (AT1) receptor blockers (ARB) used in cardiovascular diseases like heart failure and hypertension. Except for its AT1-antagonism, another mechanism of drug action has been suggested in recent research. One of the supposed actions refers to the positive impact on redox balance and reducing protein glycation. Our study is aimed at assessing the antiglycooxidant properties of valsartan in an *in vitro* model of oxidized bovine serum albumin (BSA). Glucose, fructose, ribose, glyoxal (GO), methylglyoxal (MGO), and chloramine T were used as glycation or oxidation agents. Protein oxidation products (total thiols, protein carbonyls (PC), and advanced oxidation protein products (AOPP)), glycooxidation products (tryptophan, kynurenine, N-formylkynurenine, and dityrosine), glycation products (amyloid-β structure, fructosamine, and advanced glycation end products (AGE)), and albumin antioxidant activity (total antioxidant capacity (TAC), DPPH assay, and ferric reducing antioxidant power (FRAP)) were measured in each sample. In the presence of valsartan, concentrations of protein oxidation and glycation products were significantly lower comparing to control. Moreover, albumin antioxidant activity was significantly higher in those samples. The drug's action was comparable to renowned antiglycation agents and antioxidants, e.g., aminoguanidine, metformin, Trolox, N-acetylcysteine, or alpha-lipoic acid. The conducted experiment proves that valsartan can ameliorate protein glycation and oxidation *in vitro* in various conditions. Available animal and clinical studies uphold this statement, but further research is needed to confirm it, as reduction of protein oxidation and glycation may prevent cardiovascular disease development.

Fig. 4 – Pleiotropic properties of valsartan

Statistical analysis

- The analysis was conducted using GraphPad Prism 8.3.0 for MacOS
- Differences between groups were assessed with ANOVA followed by Tukey's test
- $p<0.05$ was considered as statistically significant

Protein oxidation - results

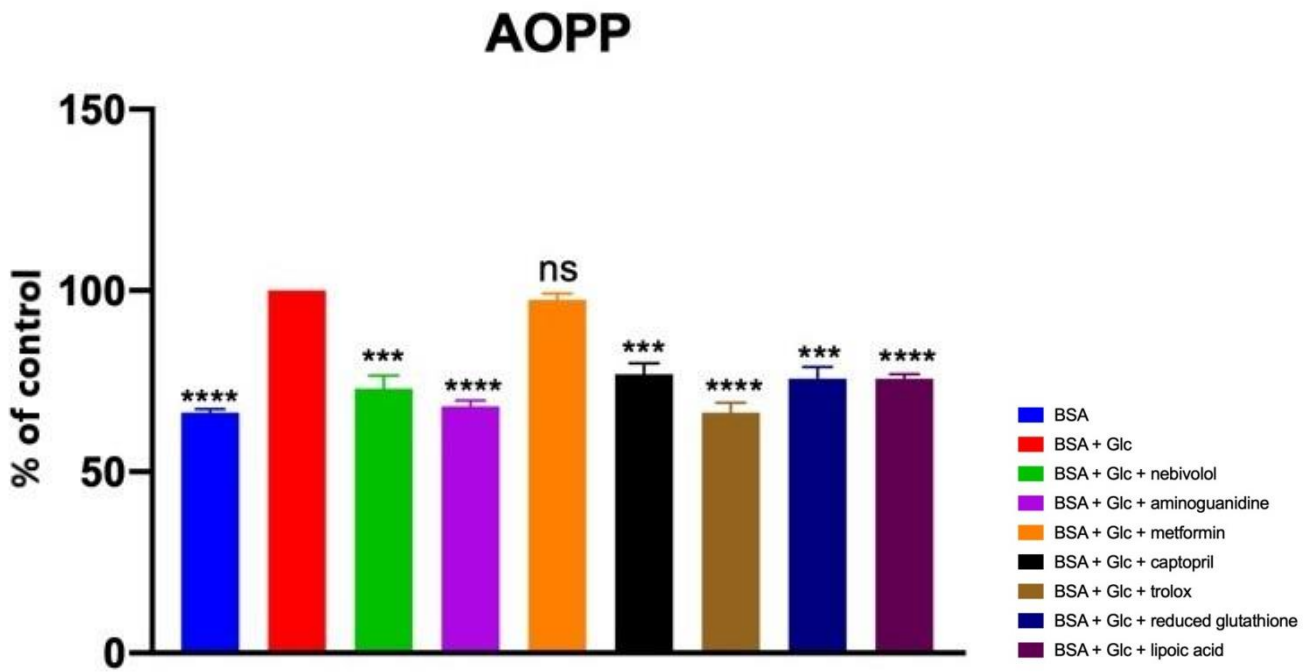

Fig. 5 – The concetration of advanced oxidation protein products (AOPP); *** $p < 0.001$ vs. control; **** $p < 0.0001$ vs. control.

Protein oxidation - results

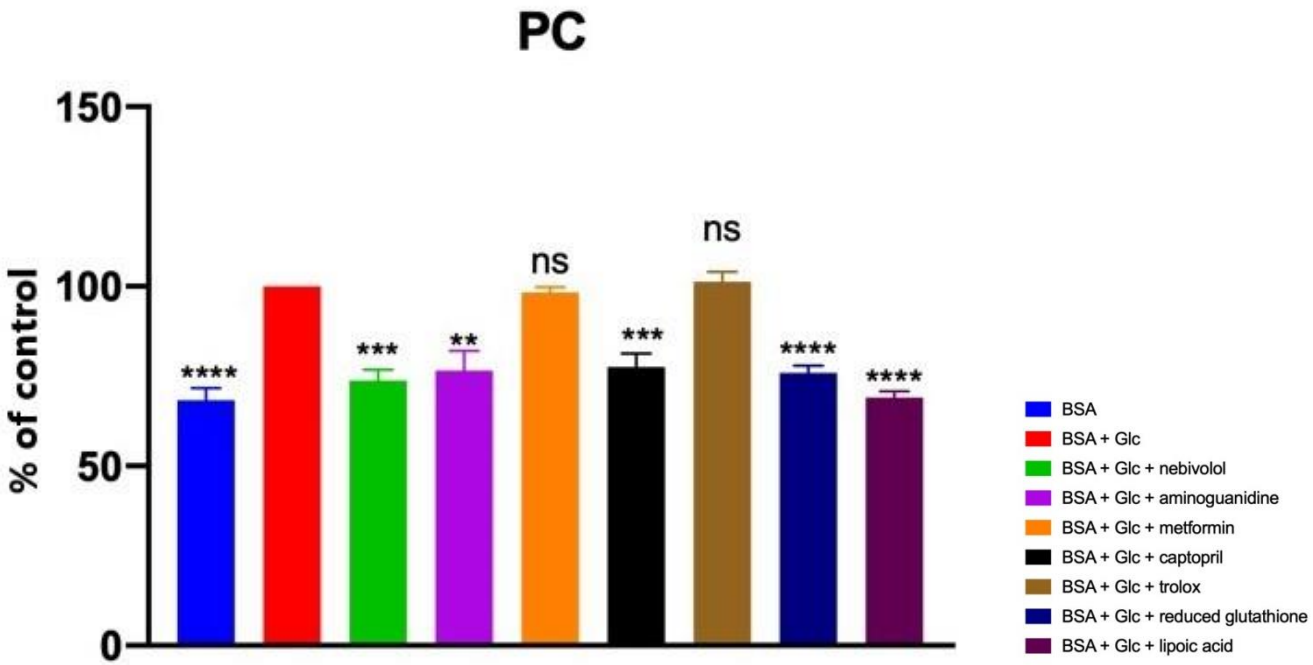

Fig. 6 – The concentration of carbonyl groups (PC);
** $p < 0.01$ vs. control; *** $p < 0.001$ vs. control; **** $p < 0.0001$ vs. control

Protein oxidation - results

- The concentration of AOPP and PC was significantly lower in samples containing nebivolol than in the samples with BSA and glucose without this drug.

- Nebivolol was more effective in preventing protein oxidating than other substances used in this study.

Protein glycation - results

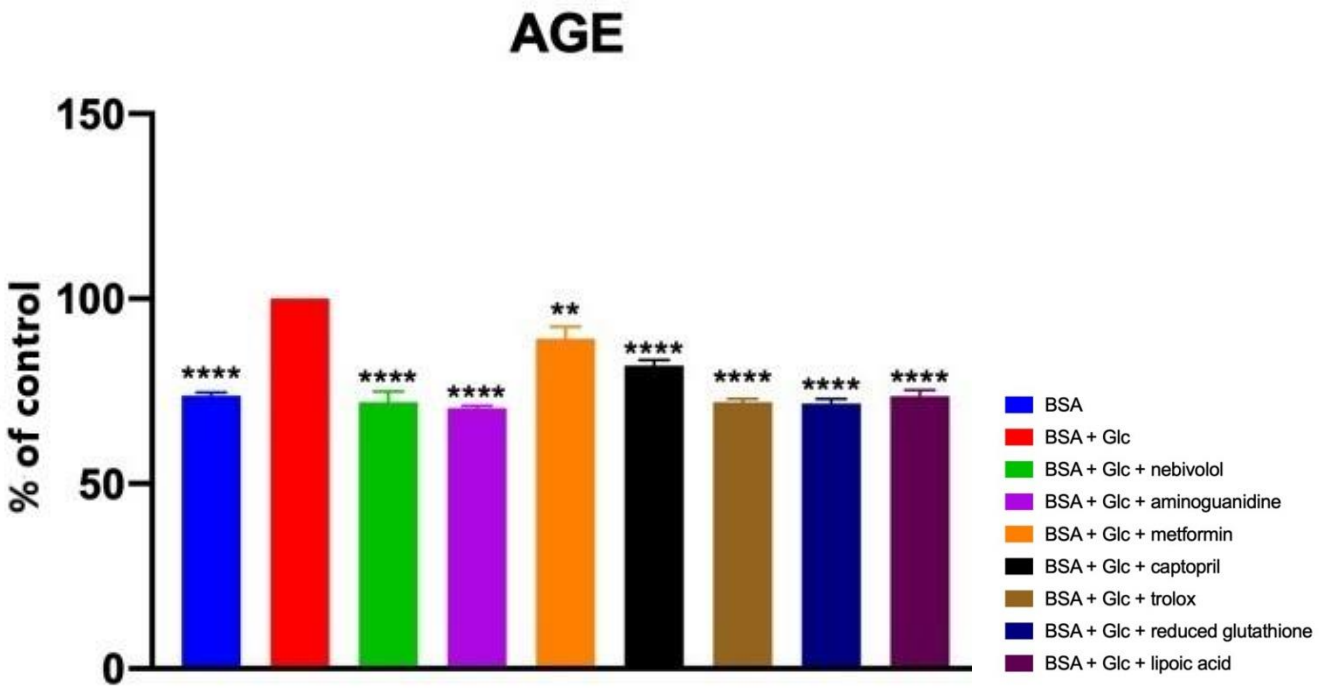

Fig. 7 – The levels of advanced glycation end products (AGEs);
** $p < 0.01$ vs. control; *** $p < 0.001$ vs. control; **** $p < 0.0001$ vs. control

Protein glycation - results

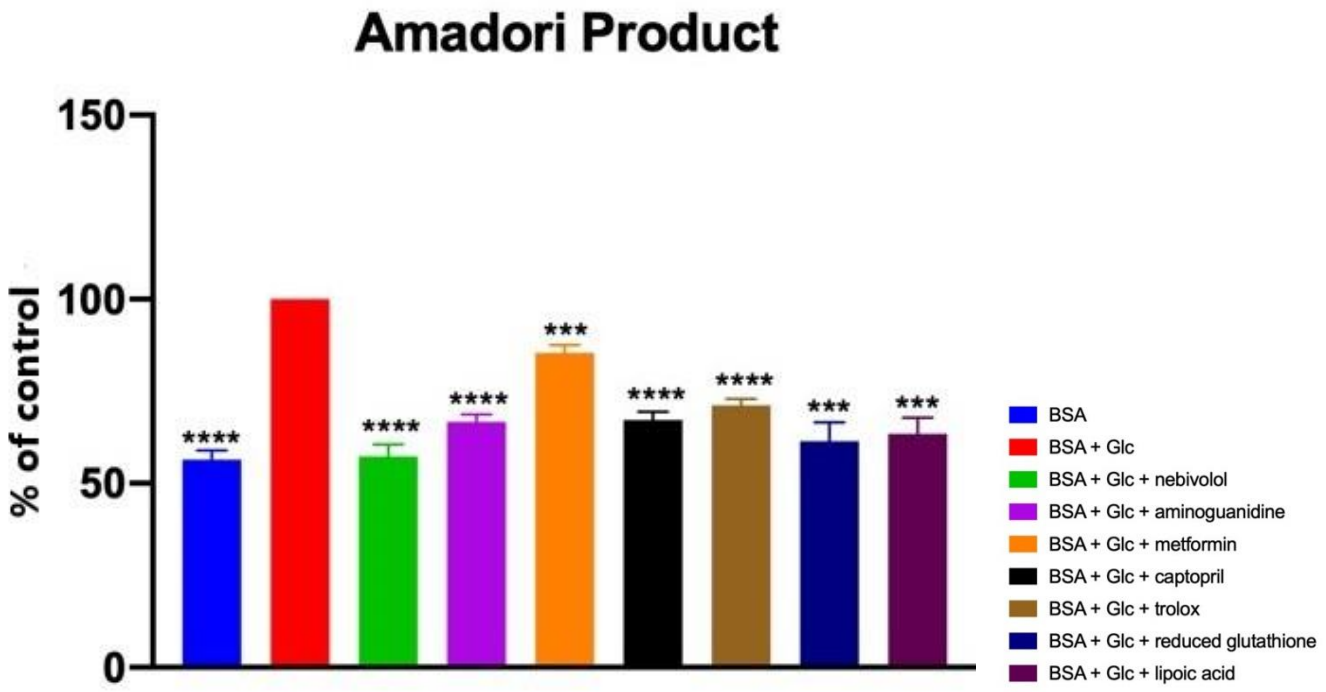

Fig. 8 – The levels of Amadori Product;
*** $p < 0.001$ vs. control; **** $p < 0.0001$ vs. control.

Protein glycation - results

- The levels of AGE and Amadori product were significantly lower in presence of nebivolol than in solutions without investigated drug

- The level of protein glycation markers were also lower in samples with nebivolol than in samples with metformin – well-known antiglycation agent

Protein glycooxidation - results

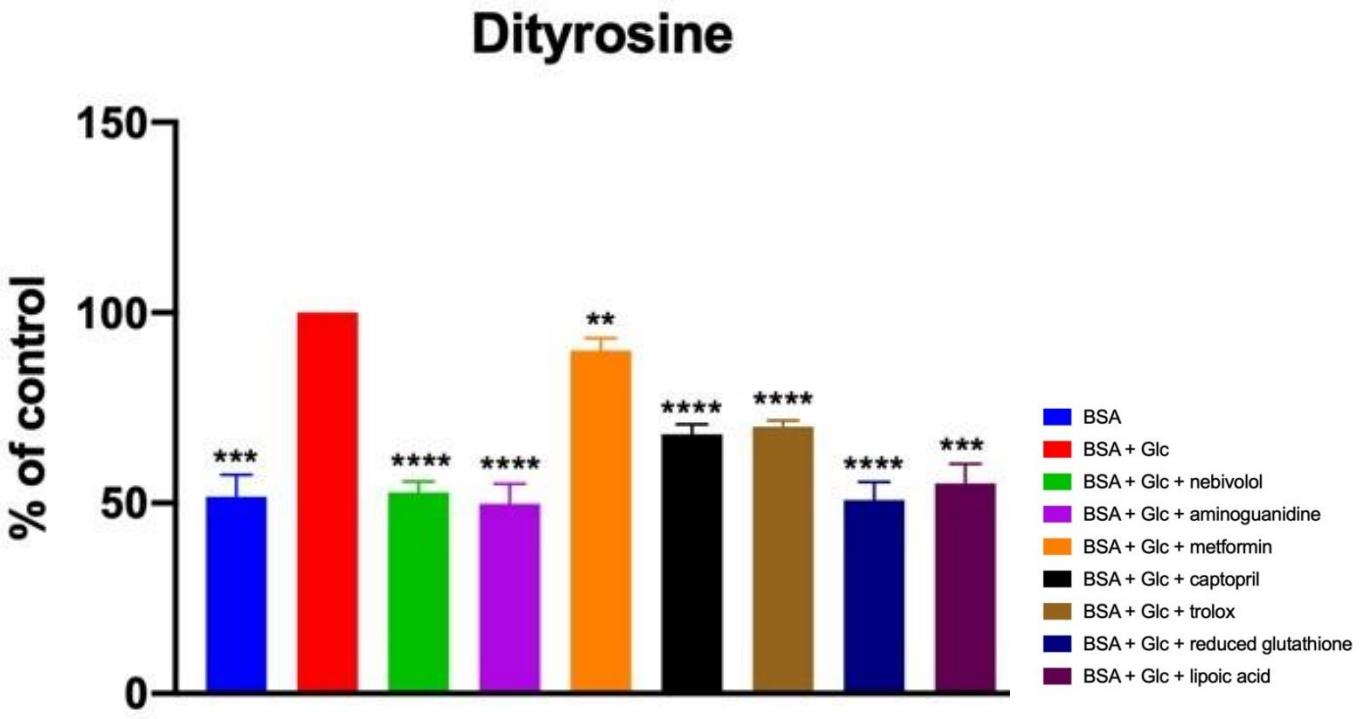

Fig. 9 – The levels of dityrosine;
** $p < 0.01$ vs. control; *** $p < 0.001$ vs. control; **** $p < 0.0001$ vs. control

Protein glycooxidation - results

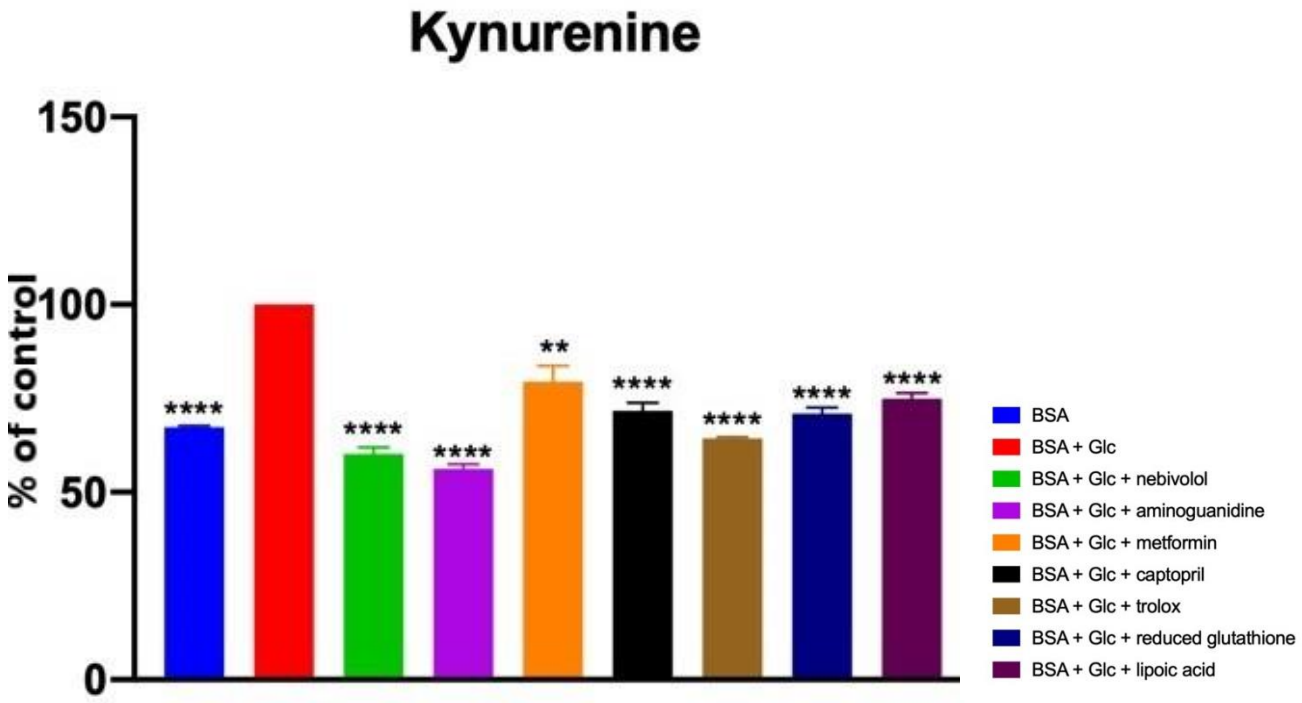

Fig. 10 – The levels of kynurenine;
** $p < 0.01$ vs. control; *** $p < 0.001$ vs. control; **** $p < 0.0001$ vs. control

Protein glycooxidation - results

- Significant decrease of glycooxidation markers was observed in presence of nebivolol
- The levels of dityrosine and kynurenine were lower in samples with nebivolol comparing to samples containing metformin

Findings

- The results of our study show that nebivolol has antiglycating and antioxidant properties in *in vitro* model
- It is necessary to conduct such studies in animal and human model
- Proving the antiglycooxidant activity of well-known and widely used drugs may lead to the breakthrough in treatment of cardiovascular diseases

References

- Videira PAQ, Castro-Caldas M. Linking Glycation and Glycosylation With Inflammation and Mitochondrial Dysfunction in Parkinson's Disease. Front Neurosci. 2018 Jun 7;12:381. doi: 10.3389/fnins.2018.00381. PMID: 29930494; PMCID: PMC5999786.
- Gryszczyńska B, Formanowicz D, Budzyń M, Wanic-Kossowska M, Pawliczak E, Formanowicz P, Majewski W, Strzyżewski KW, Kasprzak MP, Iskra M. Advanced Oxidation Protein Products and Carbonylated Proteins as Biomarkers of Oxidative Stress in Selected Atherosclerosis-Mediated Diseases. Biomed Res Int. 2017;2017:4975264. doi: 10.1155/2017/4975264. Epub 2017 Aug 13. PMID: 28884122; PMCID: PMC5572583.
- Sadowska-Bartosz I, Stefaniuk I, Galiniak S, Bartosz G. Glycation of bovine serum albumin by ascorbate in vitro: Possible contribution of the ascorbyl radical?. *Redox Biol*. 2015;6:93-99. doi:10.1016/j.redox.2015.06.017
- Pawlukianiec, C.; Gryciuk, M.E.; Mil, K.M.; Żendzian-Piotrowska, M.; Zalewska, A.; Maciejczyk, M. A New Insight into Meloxicam: Assessment of Antioxidant and Anti-Glycating Activity in In Vitro Studies. *Pharmaceuticals* **2020**, *13*, 240. https://doi.org/10.3390/ph13090240

Thank you for your attention.

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