Volume 13 Supplement 2
July 2023
ISSN 2211-5463

# FEBS openbio

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8-12 JULY

# FEBS 2023

## THE 47TH FEBS CONGRESS

TOURS, FRANCE


WILEY

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levels of certain enzymes in the human body, such as lactate dehydrogenase (LDH), alanine transaminase (ALT), aspartate transaminase (AST), and creatine kinase (CK) which can be a sign of tissue damage. The study included 750 COVID-19 patients with different disease severity ('mild', 'moderate', 'severe' and 'exitus letalis') after which we formed two groups (mild and severe group of patients) to analyze statistical differences. Patients were recruited at the General Hospital Tešanj, Bosnia and Herzegovina. Enzymes (LDH, ALT, AST and CK) were analyzed in blood samples using standard IFCC procedures. In our study, statistical analysis showed that LDH (646.50 (486.25 810.75)), ALT (34.00 (17.00 59.75)), AST (44.00 (26.00 69.75)) and CK (161.00 (85.00 342.50)) levels were higher in the group of patients with severe clinical picture in regard to group of patients with the mild disease severity. The results showed a statistically significant difference in LDH ($P < 0.001$), AST ($P < 0.001$) and CK ($P < 0.001$) levels between the mild and severe group of patients. On the other hand, ALT levels didn't show statistically significant difference between these two groups ($P = 0.816$). It is important to note that not all COVID-19 patients will have elevated levels of these enzymes, and elevated levels can also be caused by other conditions besides COVID-19. Monitoring the levels of these enzymes in COVID-19 patients can provide valuable information about the extent of tissue damage and the severity of the disease.

### P-08.2-89

### *Schistosoma mansoni* cathepsin C: from functional biochemical analysis to antiparasitic inhibitors

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Blood flukes of the genus *Schistosoma* cause schistosomiasis, a neglected parasitic disease that affects over 250 million people. Treatment relies on just one drug, and new therapies are needed. Our work is focused on the cysteine protease cathepsin C from *Schistosoma mansoni* (SmCC), which is involved in digestion of host hemoglobin, the most important source of nutrients. We demonstrated using functional proteomics that SmCC is present in blood-dwelling developmental stages of *S. mansoni* infecting humans (eggs, schistosomula, and adults). Gut association of SmCC in adult parasites was shown by immunofluorescence microscopy. Further, we investigated regulation of SmCC activity by synthetic inhibitors. A library of peptidomimetics with a reactive tetrafluorophenoxymethyl ketone warhead was screened in a kinetic fluorescence assay against native and recombinant SmCC. The selected hit inhibitors of SmCC activity were able to induce deleterious phenotypes in cultured schistosomes. Our results suggest that SmCC is a promising target for the treatment of schistosomiasis, and SmCC inhibitors represent potential antischistosomal drugs.

## Food and nutrition in biochemistry

### P-08.3-01

### An innovative application for reducing the amount of histamine in food: enrichment with diamine oxidase

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Histamine intolerance is seen in approximately 1–3% of the population. Diamine oxidase is an enzyme that oxidizes diamines such as histamine and primary monoamines. Since bacterial enzymes increase histamine formation, foods treated with microbial production or fermentation, and foods with plenty of protein include a high amount of histamine. Persons who have low DAO activity might show cause intolerance reactions after consuming foods containing high amounts of histamine. Our aim is to enrich with DAO obtained from natural foods in order to reduce the amount of histamine found in milk and dairy products. Wheatgrass was obtained from Aegean Agricultural Research Directorate. DAO-enzyme that was purified by ammonium sulfate protein precipitation, dialysis, and column chromatography steps, were added at the beginning of the fermentation step of yogurt. Samples without DAO were used as controls. After a 24-h incubation period, histamine levels of samples were determined by LCMS/MS. While enzyme activity of wheatgrass homogenate was 0.0075 U/mg, it increased up to 1046.25U/mg after column-chromatography which is the last of the extraction steps. Histamine content decreased by 42% (with 100 U/mL) and 70% (with 200 U/mL) when compared to samples without DAO. This innovative method which was applied for the first time by our group (Patent application no: 2021/010839) showed that the histamine level of yogurt was significantly reduced with DAO-enzyme sourced herbal nature. By spreading this innovative method to other foods, it will be possible for people with histamine intolerance to safely consume foods that cause intolerance. *The authors marked with an asterisk equally contributed to the work.

### P-08.3-02

### Effects of sugars on thermal and high-pressure stability of C-phycocyanin from *Arthrospira platensis*

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C-phycocyanin (C-PC), a blue, light-harvesting protein from *Arthrospira platensis*, is known for industrial application as a food colourant. However, thermal treatment has detrimental effects on C-PC colour due to sensitivity to high temperatures; therefore, its application in the food industry is limited. Hence, stabilisation of the C-PC structure by adding small, food-derived


FEBS Open Bio 13 (Suppl. S2) (2023) 61–258 DOI: 10.1002/2211-5463.13646

molecules (e.g. sugars) or applying an alternative approach to thermal treatment, such as high-pressure (HP), may allow broader use of this protein. We aimed to study HP and thermal stability of C-PC in the presence of selected sugars (glucose, fructose and sucrose). *Ex-situ* absorption spectroscopy showed that 18% of glucose, sucrose and fructose solutions, upon incubation at 65°C, exhibit higher colour preservation (91.4, 52.9 and 52.5%, respectively) in comparison to the control (46.9%). HP treatment of C-PC at 450 MPa in 18% solutions of glucose, sucrose and fructose showed 90.1, 93.2 and 74.2% of residual absorbance, respectively, while the HP treatment of control gives 82.3% of residual absorbance. *In situ* thermal fluorescence measurements revealed that free C-PC has a melting point (Tm) of 55.4°C. In comparison, glucose and sucrose increase Tm of C-PC to 64.4 and 61.4°C, respectively, while fructose does not significantly influence C-PC melting point. *In situ* HP fluorescence study confirms the stabilisation effects of sugars: the transition pressure ($P_{1/2}$) of C-PC (230 MPa) is increased in the presence of glucose (277 MPa), sucrose (304 MPa) and fructose (273 MPa). These results showed that HP treatment has significantly less detrimental effects on C-PC colour stability than thermal treatment, and the overall stability of C-PC is substantially increased in the presence of sugars. By contrast, the sugar type determines the stabilisation effect's extent. Consequently, HP treatment of C-PC-containing food could provide an alternative to thermal processing to avoid losing vivid blue colour. *The authors marked with an asterisk equally contributed to the work.

## P-08.3-03
## Molecular mechanisms of heart failure modulated by nutraceuticals in iPSC-derived cardiac models

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Induced pluripotent stem cells (iPSCs) are an interesting resource for obtaining *in vitro* cardiac models in order to investigate cardiovascular diseases. In particular, endothelin-1 (ET1) stimulation can mediate many processes associated with heart failure. Indeed, we set up monolayer and organoid cardiac models starting from human iPSCs and we found that ET1 increased the expression of hypertrophy markers (as assessed by Real-Time RT-PCR of Natriuretic Peptide A and B and Actin Alpha 1). To verify their ability to modulate key molecular pathways stimulated by ET1, we selected some diet-derived compounds (nutraceuticals): epigallocatechin gallate (EGCG), spermidine (SPD), oleuropein (OE) and quercetin (QUE). As protein misfolding and the deposition of pre-amyloid oligomers may be responsible for cellular toxicity in many cardiovascular conditions, we have addressed this issue in our model. We found that ET1 is able to induce aggregates (evaluated by Thioflavin T assay and filter assay) and nutraceuticals appear to decrease their accumulation following this stimulus. Exploring the events leading to protein aggregation, our data suggest that these nutraceuticals may influence the proteostasis of cardiac organoids by different mechanisms including autophagy promotion, aggregation or misfolding inhibition, and antioxidative action. In particular, some of these compounds seem to increase AMPK phosphorylation. Moreover, we found that ET1 impaired autophagy turnover, and the co-treatment with nutraceuticals rescued it, as assessed by LC3-II accumulation in the presence or absence of chloroquine. The present research, funded by the Fondazione Carisbo, has so far highlighted the possibility of expanding current knowledge of the molecular mechanisms exerted by nutraceutical compounds in the cardiovascular context using these study models.

## P-08.3-04
## Robinetin, a plant flavonol, exerts lipid-lowering effects by modulating histone acetyltransferase p300 in hepatocytes

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Robinetin, a plant-derived flavonol found in *Acacia mearnsii* (black wattle) and *Intsia bijuga* (Borneo teak), has been shown to possess bioactive properties. However, the inhibitory effect of robinetin on lipid accumulation and the underlying mechanism of action remain unknown. In this study, we investigated whether robinetin reduces lipid accumulation and is associated with epigenetic regulation such as histone acetylation. To investigate the effect of robinetin on histone acetyltransferase (HAT) activity at various concentrations, a HAT assay was performed in a cell-free system using HeLa cell nuclear extract as the source of HAT enzymes. Robinetin significantly inhibited HAT activity *in vitro*. To examine the inhibitory effect of robinetin on specific HATs, a HAT assay was performed using p300 recombinant enzyme instead of nuclear extracts. Robinetin significantly inhibited p300 acetyltransferase activity in a dose-dependent manner. Furthermore, in the murine hepatocyte cell line AML12, robinetin decreased oleic acid- and palmitic acid-induced lipid accumulation during lipogenesis, and lipogenesis-related gene expression of Peroxisome proliferator-activated receptors gamma 2 (PPARγ2), CCAAT enhancer binding protein beta (Cebpβ), and Liver X receptor alpha (LXRα). Docking simulation revealed that the robinetin-p300 complex could inhibit p300 activity. The benzenetriol moiety of the docking structure formed hydrogen bonds with the amino acids R1410 and T1411, whereas the phosphate group of Lys-CoA formed hydrogen bonds in the crystal structure. Our findings revealed that the inhibitory effect of robinetin on lipid accumulation is mediated by the inhibition of HAT p300. Therefore, robinetin may act as an epigenetic modulator of gene expression in lipid metabolism.

## P-08.3-05
## The effect of spermidine supplementation on survival, average lifespan and oxidative stress in honey bees (*Apis mellifera* L.)

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Honey bee (*Apis mellifera* L.), one of the most important pollinators on the planet, provides a vital service to the ecosystem that