**Supplementary file**

**Supplementary Table 1. Sequences of primers used for qRT-PCR**

| **Gene** | **Forward primer 5′–3′** | **Reverse primer 5′–3′** |
| --- | --- | --- |
| GAPDH | TGCACCACCAACTGCTTAG | GGATGCAGGGATGATGTTC |
| GSK3α | AATCTTGGCCAGTCTGAGCT | TCAGTCCTGGTGAACTGTCC |
| GSK3β | TCCATTCCTTTGGAATCTGC | CAATTCAGCCAACACACAGC |
| Akt | GGCTGCTCAAGAAGGACCCTAC | GGTGCTGCATGATCTCCTTGG |
| IL-1β | TGTAATGAAAGACGGCACACC | TCTTCTTTGGGTATTGCTTGG |
| IL-6 | ACTCACCTCTTCAGAACGAATTG | CCATCTTTGGAAGGTTCAGGTTG |
| IL-15 | CCATCCAGTGCTACTTGTGTTTAC | CCAGTTGGCTTCTGTTTTAGGAA |

**Supplementary** **Table 2. Primary antibodies used in the Western blot assay**

| **Antibody** | **Dilution** |
| --- | --- |
| Anti-β-tubulin (Abcam, Cambridge, MA, USA) Ab8227 | 1:700 |
| Anti-IL-6 (Abcam, Cambridge, MA, USA) Ab208113 | 1:1000 |
| Anti-GSK-3β (Abcam, Cambridge, MA, USA) Ab32391 | 1:1000 |
| Anti- GSK-3a (Abcam, Cambridge, MA, USA) Ab40870 | 1:1000 |
| Anti-IL-1β (Abcam, Cambridge, MA, USA) Ab9722 | 1:1000 |
| Anti-IL-15 (Abcam, Cambridge, MA, USA) Ab7213 | 1:500 |
| Anti-AktpSer473 (Abcam, Cambridge, MA, USA) Ab81283 | 1:5000 |

**Gas chromatography mass-spectrometry analysis of SHC**

Using extraction of derivatives, gas chromatography mass-spectrometry (GC-MS) analysis of SHC was carried out.

*Extraction with ethyl acetate*. 100 μl of SHC was placed into a glass vial with a screw cap, 1.0 ml of ethyl acetate (test material / solvent ratio = 1/10) was added, the mixture was thoroughly vortexed. The vial is placed on a hotplate and heated at 50° C for 24 hours. Thereafter, 200 μl of solution was centrifuged at 12000 rpm (4° C) for 10 min. Supernatant was used for further analyses.

*Extraction of derivatives*. 20 μL of a mixture of N,O-bis (trimethylsilyl) trifluoroacetamide (BSTFA) and trimethylchlorosilane (TMSC) (BSTFA to TMSC ratio was 99:1) was added to 20 μL of the supernatant. This mixture was placed on the hotplate at 75° C for 60 minutes. 70 μl of ethyl acetate was added, stirred and used for further analyses.

The GC-MS analysis was performed on a Chromatek GC-MS analyzer, consisted of a Chromatek-Kristall 5000 gas chromatograph and a DAZH-2M (3D) dispenser (Chromatek ltd., Yoshkar-Ola, Russia). Capillary column Phenomenex ZB-DRUG-1 (Phenomenex ltd., Aschaffenburg, Germany) with parameters: 30 m x 0.25 mm x 0.25 μm was used. Mass-spectrometry detector conditions were: stream division 5.0; ion source temperature 200°C; transition line temperature 290°С; scanning range = 50-550 atomic mass unit; sample volume 1 μl. For the identification of derivatives, an automatic database gas chromatography-mass spectrometry NIST14 MS Library (Adaptas SIS Ltd., Palmer, MA 01069. USA) was used. The main results of gas chromatography mass-spectrometry analysis are presented in a Table 4 of the main text.

# Summary of reported physiological effects of SHC main chemical components

Chemical analysis of the sample via GC–MS revealed prevalence of three monosaccharides: alpha-methylglucoside (39.4%), methyl beta-galactoside (9.5%), and fructofuranose (5.5%) – all of which are commercially exploited in food industry, and in low amounts are overly biologically inactive. These monosaccharides are broadly used for gustatory properties or / and crystallizing and surfactant agents in food industry that is approved by the FDA (Food and Drug Administration of the USA). Particularly, alpha-methylglucoside (aMG) is known to be a non-metabolizable glucose analog (López-Yoldi et al., 2016; Veyhl-Wichmann et al., 2016), acting as a reward for flavor preference in mice (Zukerman et al., 2013). As for methyl beta-galactoside (MbG), its physiological role in humans is not proven, while indirect effects MbG via gut microbiome can be suggested by the data showing its metabolic role in Escherichia coli and Lactobacillus (Mukai et al., 1998; Sahin-Tóth et al., 2002). In humans, D-fructofuranose (also known as fructose), is metabolized almost completely in the liver, it does not serve as a primary source of energy being is predominantly transformed into triglycerides and fatty acids (Mayes, 1993) and used in food industry as the sweetener (Malik and Hu, 2015).

Apart from three monosaccharides that were found to be the most abundant components of the SHC, six elements were found in the SHC at the concentrations exceeding 1% of the total dry weight of the sample. Among them is D-ribofuranose, which accounted for 2.5% of the total dry weight of the sample, which exists as two enantiomers: alpha-D-ribofuranose (aDR) and beta-D-ribofuranose (bDR). aDR has been widely utilized for synthesizing nucleotide and nucleoside analogs with a wide spectrum of biological effects. For example, some aDR derivatives demonstrated a powerful antinociceptive effect in mice (Petrelli et al., 2017). In line with these findings, Rahman et al. have discovered analgesic and anti-inflammatory activities in several aDR-based substances (Rahman et al., 2020). Nucleoside analogs have also been widely used in cancer chemotherapy as inhibitors of enzymes involved in intracellular nucleoside metabolism (Galmarini et al., 2002). bDR was suggested to exert immunostimulatory properties and was studied as an element of traditional Chinese medicine (Ota et al., 2019).

Another constituent of the sample was β-D-lactose (bDL), a disaccharide consisting of galactose and glucose, whose primary source is cow milk. The most recent comprehensive review by Schaafsma sums up all information available for lactose, highlighting its fiber-like activities and positive effects on absorption of minerals (Schaafsma, 2008), particularly on calcium and magnesium (Abrams et al., 2002).

The dry sample of SHC was constituting 2% of glucose, which can be found in most plant-based and animal products, either individually or, most frequently, incorporated into complex molecules, e.g., oligo- and polysaccharides. Low glucose content in the sample studied suggests its primary plant origin in the SHC and makes unlikely the possibility of any specific physiological effects of reported glucose amount on CNS or metabolism in a current study (Mergenthaler et al., 2013).

Malic acid (MA; 3.2% of the total dry weight of the sample) was postulated to show promising adaptogenic properties in 1988 by Dunaev et al. They discovered that this substance, found in various fruits, particularly citruses, promoted neuron excitation in sensory and motor brain areas in a dose-dependent manner (Dunaev et al., 1988). The observed effects were attributed to metabolism stimulation with simultaneous decrease in tissue respiration, since MA is involved in CAC (citric acid cycle), and introduction of MA into the cell thus replenishes the pool of substrate for further oxidation with less oxygen-dependent stages during the CAC. MA is also involved in malate-aspartate shuttle responsible for NADH transport across mitochondrial membrane utilized for energy production. Owing to its biological effects in energy-demanding cells, e.g., neurons and muscle cells, possible advantages of malic acid supplementation have been under investigation, generally yielding positive results (Bendahan et al., 2002; Qiang, 2015). Particularly curious results were obtained when studying the effects of MA in rat myocardial ischemia, where it exhibited cardiomyocyte-protective action, thus upholding conclusions made by other scholars (Tang et al., 2013).

Glyceric acid (GA) is a precursor of serine, an amino acid essential for neuronal metabolism, including protein and nucleotide synthesis, neurotransmitter synthesis and lipids (Tabatabaie et al., 2010). A deficiency of D-glycerate 2 kinase, an enzyme responsible for GA phosphorylation, has been associated with severe infantile epileptic encephalopathy as a result of D-glyceric acidemia (Zehavi et al., 2019). Additionally, some of GA’s phosphate derivatives (e.g., 2-phosphoglyceric acid, 3-phosphoglyceric acid, 2,3-bisphosphoglyceric acid, and 1,3-bisphosphoglyceric acid) are involved in glycolysis either directly or as regulatory molecules.

Much like MA, citric acid (CA) is involved in CAC and, therefore, energy generation in cells. CAC substrates have been shown to prevent death of ischemic neurons and astrocytes (Ying et al., 2002). Further studies by Abdel-Salam et al. have demonstrated CA’s neuroprotective effects in models of oxidative stress (Abdel-Salam et al., 2014) and malathion intoxication (Abdel-Salam et al., 2014). It is hypothesized that the underlying CA’s activities rely on the same mechanism that those of MA’s, following the logic of them both being involved in CAC. The summary of main Functions of SHC chemical ingredients in human physiology are presented in a Table 3 of the main text.

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