**Extracted Data – Neuroinflammation and crossing the blood-brain barrier**

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***1. Introductory information***

The Extracted Data – Neuroinflammation dataset and the Extracted Data – BBB dataset contain data collected from research articles that met the eligibility criteria present in the protocol referring to the systematic review with meta-analysis titled *Estimating the effectiveness of linoleic acid-isomers supplementation and NSAIDs against neuroinflammation*, which has been submitted to the *Critical Reviews in Food Science and Nutrition*. The dataset is being made public both to act as supplementary data for publication and for other researchers to use this data in their own work.

The data in this dataset was collected using computer equipment and software provided by the Laboratory of Advanced Analysis in Biochemistry and Molecular Biology of the Biochemistry Department – Chemistry Institute, between July 2021 to October 2021. An update of the search in databases occurred from January 2023 to February 2023. This review was made due to the scholarship granted from the Fundação de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPERJ).

***2. Purpose of data collection***

The purpose of data collection in Extracted Data – Neuroinflammation dataset was to investigate the anti-neuroinflammatory potential of diet fatty acids (linoleic acid and its conjugated isomers), as well as of nonsteroidal anti-inflammatory drugs (ibuprofen and aspirin) in alleviating neuroinflammation *in vitro* and *in vivo* animal models and human clinical trials. The purpose of data collection in Extracted Data – BBB dataset was to investigate the potential of diet fatty acids (linoleic acid and its conjugated isomers), as well as of nonsteroidal anti-inflammatory drugs (ibuprofen and aspirin) to cross the blood-brain barrier *in vivo* animal models and human clinical trials.

***3. Methodological information***

The population, intervention, comparison, and outcome (PICO) method has been employed for the development of the focus questions. The tool called StArt (State of the Art through Systematic Review, version 3.3 BETA) has been employed to apply the previously prepared protocol. Search strings have been constructed and adapted for five electronic databases: Science Direct, Pubmed, Embase, Scopus, and Wiley Online Library. They were related to compounds' effects on neuroinflammation, their potential to cross the BBB, and their side effects in the neuroinflammatory diseases' context.

We removed the time filter so as not to limit the number of manuscripts resulting. After, two authors independently conducted the preliminary selection of identified abstracts, titles, and keywords of research articles published in English. In the initial screening step, abstracts have been removed if the papers did not investigate anti-inflammatory therapy for neurodegenerative diseases. Papers on nonsteroidal anti-inflammatory drugs other than ibuprofen or aspirin or their derived forms were excluded. Editorials, hypothetical and modeling studies, letters, reviews, commentaries, monographs, books, preprints, and Ph.D. thesis have been removed. Based on the entire reading of the paper, all studies included in the systematic analysis were controlled experiments with a quantitative approach to data analysis. Studies whose statistical differences between treatments were not described in the text or signalled in the results were disregarded. Only studies whose treatment with an inflammatory insult was contrasted with the negative control were included. Direct neuroprotective effects *in vitro*, animal *in vivo*, or human clinical trials but without evaluating the inflammatory mechanisms involved were removed, as well as studies investigating the compounds of interest on neuroinflammation, but in the peripheral nervous system and not in the central nervous system. Side effects only in the neuroinflammatory diseases' context were included, while blood-brain barrier crossing *in situ* and *in vitro* was removed.

The determination of log BB was performed by *in vivo* animal experiments as follows:

LogBB = log [cbrain / cblood]

where cbrain is the concentration of the compound in the brain and cblood is the concentration of the compound in the blood.

***4. Data specific information***

*4.1 Extracted Data – Neuroinflammation dataset*

The data included in the Extracted Data – Neuroinflammation dataset has been organised per tested compounds. The files follow the nomenclature system below according to the organization of the spreadsheet:

Column A: Purpose of the experimental test carried out.

Column B: Definition of the tested compound.

Column C: Research article from which data was extracted.

Column D: Definition of the experimental analysis carried out in the study.

Column E: Classification of the experimental model of the extracted study (*in vitro*, *in vivo* or *ex-vivo* animal model) and human clinical trials.

Column F: Administered concentration of the tested compound.

Column G: Time the tested compound was administered in the animal model of disease or in human clinical trials.

Column H: Values obtained for analyzes regarding the control group (without therapeutic intervention). The units of measurement are presented in comments in each cell in that Excel column.

Column I: Values of standard deviation or standard error of the mean obtained for analyzes regarding the control group (without therapeutic intervention).

Column J: Values obtained for analyzes regarding the group treated with nonsteroidal anti-inflammatory drugs or linoleic acid-isomers. The units of measurement are similar to those reported for the corresponding control group in the Column H.

Column K: Values of standard deviation or standard error of the mean obtained for analyzes regarding the group treated with nonsteroidal anti-inflammatory drugs or linoleic acid-isomers.

Column L: Number of analytical or experimental replicates used in the analysis.

Column M: It informs whether or not there was a statistically significant difference between the treated group and the control group (without therapeutic intervention).

Column N: It informs whether the numerical difference between the analysis values between the treated group and the control group (without therapeutic intervention) was favorable or not in terms of mitigating neuroinflammation.

Column O: Pertinent comments to be used in the discussion of the systematic analysis.

Definition of acronyms

bw: Body weight; BDL: Bile duct ligation; NF-kB: nuclear factor kappa B; IL: interleukin; TNFα: Tumor necrosis factor alpha; GSSG: oxidised glutathione; GSH: reduced glutathione; PGE2: E-2 prostaglandin; MDA: Malondialdehyde; BDNF: Brain-derived neurotrophic factor; LPS: Lipopolysaccharide; IFN-γ: Interferon-gama; COX-2: Cyclooxygenase 2; iNOS: Inducible nitric oxide synthase; eNOS: Endothelial nitric oxide synthase; MCP-1: Monocyte chemoattractant protein 1; MIP-2: Macrophage inflammatory protein; GFAP: Glial fibrillary acidic protein; TREM: Triggering Receptor Expressed on Myeloid cells; ROS: Reactive Oxygen Species; Iba1: Ionized Calcium-binding adaptor molecule 1; JNK: c-Jun N-terminal kinase; SFA: LOOH: lipid hydroperoxide; SOD: superoxide dismutase; LA: Linoleic acid; CLA: conjugated linoleic acid-isomers; BBB: Blood brain barrier; VCAM-1: Vascular cell adhesion molecule 1; MPO: myeloperoxidase activity; IkB: IkappaB kinase; Str/BF: Striatum and basal forebrain at rostral striatal level; ICE: interleukin-1b converting enzyme; IL-1 ra: Interleukin-1 receptor antagonista; ATL: Aspirin-triggered lipoxin; NPAs: Neutrophil/platelet aggregates; MMP-2: Matriz metalloproteinase-2; MMP-9: Matriz metalloproteinase-9; NOX1: NADPH oxidase 1; NOX2: NADPH oxidase 2; IL-1β: Interleukin 1 beta; MIP1a: Macrophage inflammatory protein-1 alpha; TNFR1: Tumor necrosis factor receptor 1; MTT: (3-(4, 5-dimethylthiazolyl-2)-2, 5- diphenyltetrazoliumbromide); LDH: Lactate dehydrogenase; 8-iso-PGF2α: 8-iso-prostaglandin F2α; CRP: C-Reactive Protein; Nac: nucleus accumbens; PFC: prefrontal cortex; Aβ: β-Amyloid Peptide; ZO-1: Zonula occludens-1; IgG: Immunoglobulin G; AchE: acetylcholinesterase; SNpc: Substantia nigra pars compacta; Al: Aluminum; RCR: Respiratory control ratio; V4: oxygen consumption in the resting state of mitochondrial respiration; GCL: γ Glutamylcysteine ligase; GSR: Glutathione reductase; G6PD: Glucose 6 phosphate dehydrogenase; GST: Glutathione-S-transferase; GPx: Glutathione peroxidase; CXCL-1: The murine homolog of human IL-8; Nrf2: Nuclear erythroid-related factor 2; dMBP: Damaged myelin basic protein; WT: wild type; LKO: Epm2a-/-, laforin knockout; MKO: Nhlrc1-/-, malin knockout; PPARγ: Peroxisome proliferator-activated receptor γ; SD: Standard deviation; SEM: standard error of the mean; A.U: Arbitrary unit; CPM: counts/min per mg wet weight; ^: Exponentiation; Thio S: Thioflavin-S; AT100: Tau (AT100).

*4.2 Extracted Data – BBB dataset*

The data included in the Extracted Data – BBB dataset has been organised per tested compounds. The files follow the nomenclature system below according to the organization of the spreadsheet:

Column A: Purpose of the experimental test carried out.

Column B: Definition of the tested compound. In the case of isomers, the type and proportion of each of them in the formulation is also defined.

Column C: Research article from which data was extracted.

Column D: Criteria used to evaluate the potential for the compound to cross the blood-brain barrier. When the study’s experimental design made it impossible to determine the log BB, the crossing ability was evaluated by comparing the concentration of the compound in the treated animal's brain to the control animal's brain (without diet supplementation).

Column E: Description of the experimental model from the extracted study.

Column F: Administered concentration of the tested compound.

Column G: Time elapsed from administration of the tested compound to collection of target tissue for quantification of the compound therein.

Column H: To evaluate the efficiency of the compounds in crossing the blood-brain barrier, the extracted values were expressed as log BB or as the percentage ↑ in the concentration of the compound in the brain of the treated group in relation to the control group (non-supplemented diet).

Non-applicable cases (NA) refer to non-detection of the tested compound in at least one of the tissues analyzed for quantification.

Column I: Number of analytical or experimental replicates used in the analysis.

Column J: It indicates whether the result was favorable or not, being considered favorable when the compound was able to cross the blood-brain barrier.

For log BB values, the usual optimum threshold value from 0 to -1 was used in each study to define whether the compound tested reached the central nervous system.

For the remaining cases, when the concentration in the brain of the animal with the intervention was significantly higher than in the control brain, the compound was found to cross the blood-brain barrier.

Definition of acronyms

↑: increase; bw: Body weight; BBB: Blood-brain barrier; CLA: conjugated linoleic acid; AD: Alzheimer´s disease; NA: Not applied;