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Caprine milk alpha-S2 casein protein of Ethawah breeds is able to enhance biological activities related with gene susceptibility of human disease regulation

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Most of biological signaling pathway was orchestrated at the level of proteins and biological active compounds, that both molecules recognition have ability to interact and modulate molecular mechanisms underlying an organism's physiological functions. Differentiation of structural and physicochemical properties of bioactive compounds is an important factor to determine the biological function. Local Indonesian goat Ethawah breed milk is one of the nutritionally enriched dairy breed milk to provide biological function modulation without health risks. Recently in our study, we found high amount of caprine alpha-S2 casein of goat Ethawah breed milk exclusively isolated from 36 kDa, and identified the eight bioactive peptides fragments of caprine alpha-S2 casein by MALDI-TOF analysis. This study focuses on elucidating the biological function of caprine milk alpha-S2 casein protein provided by *in vitro* and *in silico* analyses. We found that alpha-S2 casein protein in high MG environment inhibits the decreasing of viability due to increase in proliferation of MC3T3E1pre-osteoblast cell. In animal model, this protein was able to down regulate cytokine pro-inflammation on some tissues target and controlled RAGE-AGE signaling pathway related with ROS and oxidative stress. These data was also confirmed by *in silico* analysis, and we detected that each bioactive peptide of caprine milk alpha-S2 casein protein displays a wide range of physiological functions as anti-inflammation, anti-oxidative, and immunomodulatory mechanism to regulate the cellular and molecular signaling mechanism to promote health life improvement.

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Estrogenic potency of bisphenol S, polyethersulfone and their metabolites generated by the rat liver S9 fractions on a MVLN cell using a luciferase reporter gene assay

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Bisphenol A (BPA) is an applied chemical that is used in many industrial fields and is a potential Endocrine Disruption Chemical (EDC) that is found in the environment. Bisphenol S (BPS) and Polyethersulfone (PES) have been suggested as putative BPA alternatives. In this study, the estrogenic potency induced by the binding of 17-beta-estradiol (E2), BPA, BPS, PES and their metabolites formed by the rat liver S9 fraction to the human Estrogen Receptor (ER) was estimated. We used an *in vitro* bioassay based on the luciferase reporter assay in MVLN cells to evaluate the estrogenic activity of 17-beta-estradiol (E2), BPA, BPS, PES (E2: 0.001 to 0.3 nM; BPA, BPS and PES: 0.0001 to 5 microM) and their metabolites (E2: 0.05 microM; BPA, BPS and PES: 0.1 mM) according to incubation times (0, 20 and 40 min). After chemical treatment to MVLN cells for 72 hrs, and the cell viability and luciferase intensity induced were estimated, from which the estrogenic activity of the chemicals tested was evaluated. BPA and BPS induced estrogenic activity whereas PES did not show any estrogenic activity in the concentrations tested. In an *in vitro* assay of metabolites, BPA metabolites displayed comparable estrogenic activity with BPA and metabolites of both BPS and PES showed increasing estrogenic activity. The results suggested that the metabolites of BPS and PES have estrogenic potential and the need for the assessment of both chemicals and their metabolites in other EDC evaluation studies. The estrogenic potency of PES and its metabolites is the first report in our best knowledge.

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