A Method for Isolation of Neuroprotective Bioactive Peptides from Fermented Fish (Telesh Shidal) and Compositions Thereof

Detailed description of the technology

The newly filed patent technology from IASST having title “A METHOD FOR ISOLATION OF NEUROPROTECTIVE BIOACTIVE PEPTIDES FROM FERMENTED FISH (TELSH SHIDAL) AND COMPOSITIONS THEREOF” (Patent application no. 202631060953, submitted on 3/05/2026) relates to the discovery, isolation, characterization, and application of neuroprotective bioactive peptides derived from a traditionally fermented fish product known as *Telsh Shidal*, consumed by ethnic communities of Northeast India. This innovation bridges traditional knowledge with modern scientific validation, establishing a robust platform for developing food-derived therapeutic molecules. Fermented foods are known to be rich sources of bioactive compounds generated through microbial proteolysis; however, the identification of specific peptides with well-defined neuroprotective properties and validated biological activity has remained limited. The present invention addresses this gap by providing a systematic and reproducible approach for isolating peptide-rich fractions and purifying functionally active peptides with demonstrated efficacy across multiple experimental models.

The technology involves the preparation of a peptide-rich substrate (PRS) from fermented fish through a sequence of homogenization, aqueous extraction, centrifugation, filtration, and lyophilisation steps. Further enrichment of low-molecular-weight peptides is achieved using ultrafiltration with a defined molecular weight cutoff. The PRS thus obtained serves as the starting material for chromatographic separation using reverse-phase high-performance liquid chromatography (RP-HPLC), which enables the isolation of two distinct bioactive peptides designated as C1 and C2. These peptides have been structurally characterized as AAADLDAALK (C1) and LEEDELKL (C2), respectively, through advanced analytical techniques including LC–MS and LC–MS/MS-based de novo sequencing, along with spectroscopic validation using UV and FTIR analysis.

The biological efficacy of these peptides has been rigorously evaluated using in vitro and in vivo systems. In PC-12 neuronal cells exposed to paraquat-induced oxidative stress, both peptides demonstrated significant neuroprotective effects by reducing intracellular reactive oxygen species (ROS), inhibiting apoptosis, and restoring cell viability. Notably, peptide C2 exhibited relatively higher intrinsic activity compared to peptide C1. Importantly, a defined synergistic combination of peptides C1 and C2 in a molar ratio of 1:2 resulted in markedly enhanced neuroprotection, achieving approximately 91.9% cell viability, thereby demonstrating a true synergistic interaction rather than a simple additive effect.

The translational relevance of the technology has been further validated in whole-organism models. In *Caenorhabditis elegans*, treatment with the peptides led to improved survival, enhanced motility, and increased resistance to oxidative stress, confirming functional neuroprotection at the organismal level. In zebrafish embryo models, evaluated under OECD Test Guideline No. 236, peptide C2 exhibited an excellent safety profile with no observable toxicity up to 200 μM, maintaining normal development, morphology, and cardiac function. Peptide C1 showed only mild toxicity at higher concentrations, thereby reinforcing the safety and applicability of the peptide system.

Mechanistically, the neuroprotective activity of these peptides is attributed to their strong antioxidant properties, ability to suppress oxidative stress, inhibition of apoptosis, and stabilization of cellular homeostasis. The peptides effectively mitigate paraquat-induced neuronal damage by modulating intracellular signaling pathways associated with oxidative stress and cell survival. The synergistic formulation further enhances these effects, making it a promising candidate for therapeutic and nutraceutical applications.

Overall, this technology represents a novel and scientifically validated approach for harnessing bioactive peptides from traditional fermented foods for neuroprotection. Its uniqueness lies in the identification of specific peptide sequences, demonstration of synergistic interaction, multi-scale validation across cellular and organismal models, and its strong potential for translation into pharmaceutical, nutraceutical, and functional food applications.

Problem solved / Applicability of the technology

Neurodegenerative disorders and neurotoxin-induced neuronal damage represent a major global health challenge, with limited availability of safe and effective therapeutic options. Existing treatments are often associated with side effects, high costs, and limited efficacy in preventing disease progression. At the same time, although fermented foods are widely recognized for their health benefits, the specific molecular components responsible for these effects are often poorly defined, limiting their translation into targeted therapeutic applications. There is therefore a critical need for natural, safe, and scientifically validated bioactive compounds that can provide neuroprotection and mitigate oxidative stress-induced cellular damage.

The present technology addresses these challenges by providing well-defined bioactive peptides derived from a traditional fermented food source, along with a reproducible method for their isolation and purification. It offers a novel solution in the form of peptide-based neuroprotective agents that are both effective and safe. The identification of a synergistic peptide combination further enhances therapeutic potential, allowing improved efficacy at lower concentrations. The technology is highly versatile and finds applicability across multiple sectors, including pharmaceutical

development of neuroprotective therapeutics, nutraceutical and functional food industries for brain health supplements, and biotechnology sectors focused on antioxidant and anti-apoptotic formulations. Additionally, it provides a scientific basis for value addition to traditional fermented foods, thereby supporting indigenous knowledge systems and promoting translational research.

Patent status

The technology has been filed as an Indian patent application through Seenergi IPR on behalf of the Institute of Advanced Study in Science and Technology (IASST), Guwahati. The filing date is 13 May 2026, Patent application no. 202631060953**,** and the current status of the application is under examination

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Graphical Image

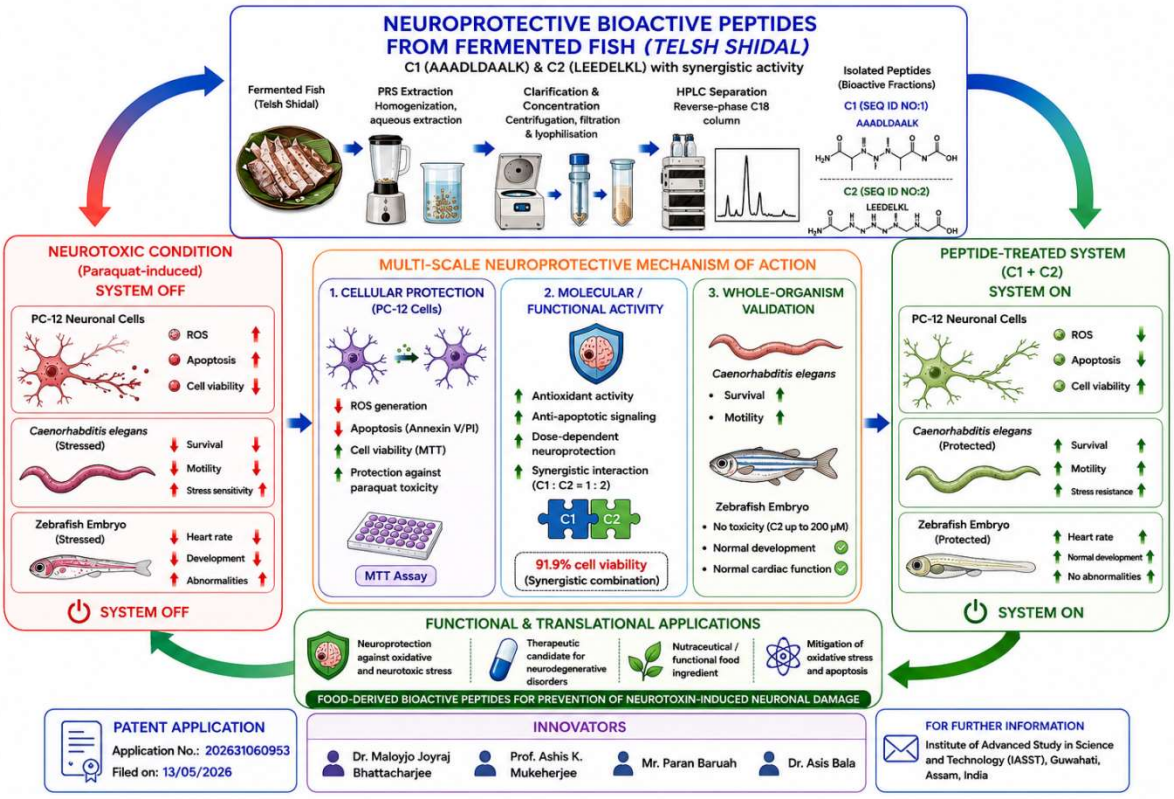

Figure: Schematic representation of the isolation and neuroprotective application of bioactive peptides (C1 and C2) derived from fermented fish (Telsh Shidal). The peptides are obtained through peptide-rich substrate (PRS) extraction followed by HPLC purification. The isolated peptides exhibit strong antioxidant and anti-apoptotic activity in PC-12 neuronal cells, and demonstrate in vivo neuroprotection in *Caenorhabditis elegans* and zebrafish models. A defined synergistic combination (C1:C2 = 1:2) provides enhanced neuroprotection, restoring cellular viability and reducing oxidative stress, highlighting its potential as a therapeutic and functional food-based intervention.