BIOLOGICAL ACTIVITY:

Cyclo(His–Pro) is a cyclic dipeptide structurally related to tyrotropin–releasing hormone.

**In Vitro:** Cyclo(His–Pro) is a cyclic dipeptide derived from the hydrolytic removal of the amino–terminal pyroglutamic acid residue of the hypothalamic thyrotropin–releasing hormone. Cyclo(His–Pro) is ubiquitous in the central nervous system and is a key substrate of organic cation transporters, which are strongly linked to neuroprotection. The cyclic dipeptide can also cross the brain–blood–barrier and, once in the brain, can affect diverse inflammatory and stress responses by modifying the Nrf2–NF–κB signaling axis\(^1\). Cyclo(His–Pro) inhibits NF–κB nuclear accumulation induced by paraquat in rat pheochromocytoma PC12 cells via the Nrf2/heme oxygenase–1 pathway\(^2\).

**In Vivo:** Mice that receives cyclo(His–Pro) pre–treatment shows a significant decrease in the oedematogenic response, confirming that the cyclic dipeptide can exert anti–inflammatory effect\(^2\). Cyclo(His–Pro) exerts in vivo anti–inflammatory effects in the central nervous system by down–regulating hepatic and cerebral TNFα expression thereby counteracting LPS–induced gliosis. Moreover, by up–regulating Bip, cyclo(His–Pro) increases the ER stress sensitivity and triggers the unfolded protein response to alleviate the ER stress\(^3\).

PROTOCOL (Extracted from published papers and Only for reference)

**Cell Assay:**\(^2\)Immortalised murine microglial BV2 cells are incubated for 24 h with 50 μM cyclo(His–Pro), and then exposed to IL–6 (5 ng/mL) for 24 h. Live cells were counted by hemocytometer and viability assessed by the conventional MTT reduction assay after washing the cells with PBS\(^2\).

**Animal Administration:** Cyclo(His–Pro) is prepared in DMSO.\(^2\) Mouse: Cyclo(His–Pro) anti–inflammatory effect is determined by topical application on the right ear of the second group (thirty C57BL/6 mice) of 1.8 mg/ear of cyclo(His–Pro) 30 min prior to TPA. Ear thickness is measured before and after induction of the inflammatory response by a micrometre\(^2\).

References:

Caution: Product has not been fully validated for medical applications. For research use only.

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