

Drug Discovery Based on Thymopentin for Treating Anxiety and Depression

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Thymopietin(TP) was originally isolated from bovine thymic extracts on the basis of its ability to affect neuromuscular transmission when injected into mice (Goldstein, 1974). A 49 amino acid polypeptide was isolated and sequenced (Schlesinger and Goldstein, 1975). It is now evident that this molecule was created by proteolytic cleavage of larger thymopietin proteins during isolation, and represents the N-terminal sequence of these proteins. Nevertheless, this proteolytic fragment was active in both neurophysiological and immunological experiments, and enabled the identification of an active pentapeptide. (amino acids 32 to 36, Arg-Lys-Asp-Val-Tyr, thymopentin), which has been studied as an immunomodulatory drug.

Now, the pentapeptide thymopentin is a well-known immunoregulatory substance. In view of the intimate bilateral communication between the nervous and immune system, involving peptide hormones and their receptors as major information messengers, the attention has been mainly focussed on the possible influences exerted by thymopentin on the functions of the central nervous system. Pharmacological and neurochemical experiments were predominantly carried out on stress models reveals dramatic changes that occur in the nervous, endocrine and immune systems in response to stress. Current concepts involving the biology of stress mechanisms suggest that physiologic responses are coordinated through a central integrated pathway involving the brain, Corticotropin Releasing Factor(CRF) and the Hypothalamic-Pituitary-Adrenal (HPA) axis.

The new molecular entity appears to be a novel agent for modifying levels of CRF, the hormone responsible for the immuno-suppressive response of the body to stress or danger. Preclinical models showed pre dosing with the compound caused changes in both behavior and secretion of CRF. Peptide drugs made of naturally occurring amino acids could provide safe alternatives for treating anxiety and depression where traditional therapies produce unwanted and hazardous side effects.

