

Research Article

Dipeptide is a Prominent in Treatment of various Diseases

Mr. Sumit Popat Nehe^{*1} and Mr. Kundan J. Tiwari²

Student, SMBT College of Pharmacy, Nandi Hills, Dhamangaon, Igatpuri, Nashik, Maharashtra, India - 422 403.

Head of Department, SMBT Institute of D. Pharmacy, Nandi Hills, Dhamangaon, Igatpuri, Nashik, Maharashtra, India – 422403.

ARTICLE INFO

ABSTRACT

Article history:

Received: 14/08/2023

Revised: 15/08/2023

Accepted: 19/08/2023

Key Words:

Comparing, Furan, Imidazole, Nicotinic Acid, Thiazide

Please cite this article as: Nehe S. *et al.* Dipeptide Is A Prominent In Treatment of Various Diseases 6(1), 24-28.

Peptides and proteins are still being used in pharmaceuticals due to their prospective use in both the market for protein drugs and current pharmacological therapy. Peptide-based medications function as antibacterial agents. The majority of synthetic compounds are designed to inhibit microbial cell multiplication. When peptides bind to heterocyclic compounds, they exhibit a variety of activities, including antibacterial, antifungal, and antiemetics properties. Over the past 20 years, a vast array of biopeptides has been identified. condensation of heterocyclic moiety with peptides that contain amino acids, such as Strong biological activity are shown by nicotinic acid, thiazole, coumarin, quinoline, furan, and imidazole, are other peptide-containing amino acids.

©2023 Published by International Journal of PharmaO₂. This is an open access article.

* Corresponding Author- **Sumit Popat Nehe**

Introduction:

Designing novel medications has long been an exciting area of scientific research and medicinal chemistry. Adding changes to the parent chemical frequently improves the compound's activity and, in most circumstances, reduces the undesirable effects or toxicity associated with the parent medication. To create a molecule that will have a certain therapeutic effect, a scientific understanding of pharmacological action is essential. Repeating terms of unit, or residues of amino acids joined by peptide bonds, also called amide bonds, peptides and proteins. [Lemke TL 2008], [Gary Hu. 2010]

The development of new pharmaceuticals has long been a fascinating topic of scientific research and medicinal chemistry. Changing the parent chemical frequently increases its activity and reduces the toxicity or side effects of the parent medication in the majority of situations. A comprehensive comprehension of pharmacological activity is necessary in order to synthesize a molecule that has a particular therapeutic effect. Repetitive units of amino acids linkage together by eupeptide bonds, sometimes called organic bonds, make up both peptides and proteins [Lemke TL 2008], [Gary Hu. 2010].

Amino acids make up proteins, and conjugated proteins contain extra elements. Though, in practice, the term "amino acid" is typically used in reference to natural sources of amino carboxylic acids, it can, in theory, refer to any of the material having an amino group and an acidic property. Commonly, amino acids have the common structure depicted below. - The atom of carbon to which the carboxylic acid group is attached is denoted by carbon. Peptides are compounds consisting of two or more amino acids joined by a peptide bond. And they are also called as amide linkage or peptide bonds. One amino acids nitrogen atom forms a unique bond with another amino acids carboxylic carbon atom. [Ansari KF, Lal C et al 2009] [Virender K. Sarin, Stephen B. H. Kent, et al 1972].

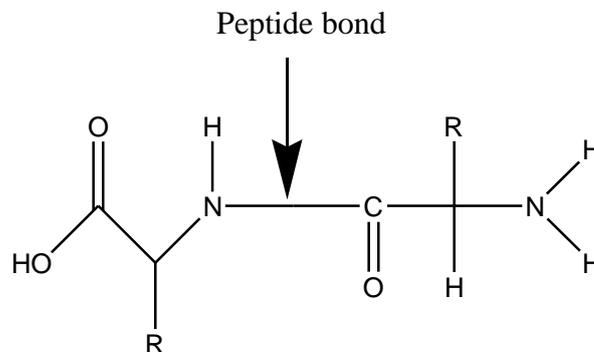


Fig: Peptide Bond

The identification of peptides as pituitary hormones significantly increased the synthesis of novel peptide derivatives as therapeutic agents. Numerous peptides have diverse biological functions, such as hormone production, enzyme activity, substrates for enzyme inhibitors, growth promotion or inhibition, neurotransmitter, and immunomodulator [Pandey R., Singh A., et al 2009], [P. Parimoo 2006].

Small amounts of peptides from natural sources are the source of most peptides used as therapeutic agents. Numerous heterocyclic compounds with biological effects, including those that are antifungal, antibacterial, antineoplastic, insecticidal, anti-inflammatory, and form melanin, have been found. Nature is full of heterocyclic compounds, which are essential to life. Heterocyclic substances like purines and pyrimidines also make up DNA. Numerous pharmacologically active and clinically used heterocyclic compounds, both natural and synthetic, have been identified [Tsume Y., Bermejo B., et al 2014], [Shinde VN, Himaja M, et al 2010]. In agriculture, a number of heterocyclic compounds are employed as pesticides, herbicides, fungicides, and so forth. In addition, they are employed as copolymers, developers, sensitizers, antioxidants, and so forth [Gupta R.R., Kumar M. et al 2005], [Shinde NV, Dhake AS, et al.2013], [Dutra LA, Melo TRF, et al.2012].

Peptide Bond Peptide synthesis, on the other hand, is the process of generating peptide molecules by joining several amino acids together with amide bonds (Lemke TL, Williams DA, Roche VF, 2008). After the water molecule is removed, two amino acids are joined together by a peptide bond, also known as peptide linkage or amide linkage. A peptide bond is a covalent bond. This is a one-of-a-kind linkage that binds the Nitrogen atom of one amino acid to the Carboxylic acid carbon atom of another atom.

Structure of Dipeptide

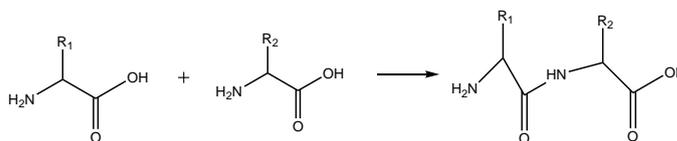
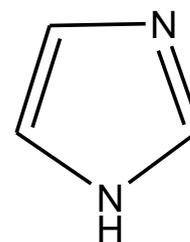


Fig: Dipeptide

Prodrug

Imidazole Prodrugs are medications that go through biotransformation prior to exhibiting their intended or increased pharmacological activity. imidazole have heterocyclic ring in that 3-carbon atom and 2-nitrogen atom. Its chemical name is 1, 3-diazole. The prodrug is mostly used in stability, solubility therapeutic effect, these are the most useful for masking the unpleasant taste of drug. The drug are used for the decrease the side effect and toxicity. (R.M.Mehata,2019)



1H-Imidazole

Chemical Formula C₃H₄N₂

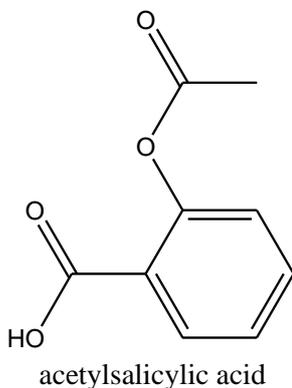
Molecular Weight 68.02gm/6ml

Melting Point 91^oC

Aspirin

Prodrugs are drugs that undergo biotransformation before achieving target pharmacological activity. It is sometimes called Pro-agent's. Prodrugs are often the ester or amide of the parent drug. Prodrugs improve drug stability, solubility, and bioavailability while masking undesirable taste and odor from the parent chemical. They help minimize drug toxicity. Prodrugs

can hide the negative effects and toxicity of drugs like aspirin. Heterocyclic compounds have diverse biological effects, including anti-inflammatory, antifungal, analgesic, antipyretic, anti-rheumatic, antineoplastic, insecticidal, and melanin formation inhibitory properties. The discovery of peptides as pituitary hormones accelerated the development of novel peptide compounds for medicinal purposes.



Solution Phase synthesis

Solution-based synthetic chemistry is the most prevalent type. Reaction conditions must be established and optimized, which takes time and resources when a reaction needs to be adjusted to make room for a solid support. In fact, a combinatorial chemist might work on a solid-phase reaction for months and gather all the necessary ingredients, just to complete the synthesis within a few hours or days. Many reactions have inadequate yields or fail miserably, making them unsuitable for execution on solid supports. These have led to a great deal of interest in combinatorial library creation using solution-phase chemistry. Combinatorial chemistry in the solution phase often results in a mixture of compounds. Think about putting ten amines and ten acid chlorides in flask, along with the adjuvant and products, and with the conditions such that only amine-chloride reactions happen instead of amine-amine or chloride-chloride reactions. [Patrick G. L.2003].

A fuse of the one hundred amides, one for each potential mixture of the amine with the acid chloride, would be the end product. Once the inactive amides have not obstructed the binding of the active molecule, the resulting combination may be assessed for activity. Slight subsets of amines along with chlorides can be examined if activity is found in order to identify the structure causing the activity. [Block JH, Beale JM, Wilson and gisvold's et al. edition10], [Malipeddi H, Malipeddiven K, et al 2010]

Only three steps are involved in solution phase synthesis, as indicated below.

First Step: Defense An acid group with an acid group on one end and a basic groups on the other is called an

amino acid. An amino acid becomes unreactive when one of these groups reacts with something else, preventing it from interacting with itself. [Virender K. Sarin, Stephen B. H. Kent, et al 1972].

Second Step: Coupling : Initially, the peptide chain is formed by a reaction between the amino acid bonded to the polymer and the protected amino acid.. [Virender K. Sarin, Stephen B. H. Kent, et al 1972].

Third Step: Deprotection: The acid at end of the chain can now react with the acid that is supplied next since the protection group is no longer present. The cycle is repeated until the required chain length is reached after the new acid has been protected . [Virender K. Sarin, Stephen B. H. Kent, et al 1972].

Solid Phase Synthesis

The stepwise approach to peptide synthesis, when carried out by conventional chemical techniques in which each intermediate is purified before next step, is of limited value for large peptide because the overall yield is very low.

The growing peptide chain is attached by chemical bond to solid support(insoluble polymer). Impurities and unused reagents can be simply removed by washing and filtration. Each step is quantitative and overall yield is high.

Steps involved

Activation of the Solid Support Typically, the solid support material (resin or polymer bead) is modified to attach the first building component (monomer). This can often be done by treating the support with a reagent containing a reactive group, such as a hydroxyl or amino group.

Coupling when the first building block, which is normally protected at reactive locations in order to avoid unexpected reactions, is chemically coupled to the activated solid support. This establishes a covalent bond between the building block and the support.

DE protection If needed, protecting groups are eliminated from reactive sites on the newly attached building block to expose functional groups to subsequent reaction.

Washing: Unwanted reagents and byproducts are removed to assure purity and avoid unwanted side effects.

Repetition: For each additional building block, steps 2-4 are performed sequentially, with coupling and DE protection cycles alternating.

Final DE protection and Cleavage After the desired sequence of building blocks has been established any remaining protecting groups are removed, and the synthesized molecule can be separated from the solid support. This phase often involves chemically treating the sample with appropriate chemicals to release the desired product while leaving the support intact.

Purification The crude product is purified using procedures such as chromatography or crystallization to separate the final desired molecule from contaminants.

Conclusion

As we see many peptides based molecule are shown the good biological activity like cytotoxic, antimicrobial, anticancer etc. The synthesized molecules even may be tested for many biological activities taking into consideration, the activities possessed by the peptide based molecules, there is a scope for the designing of new peptide molecules.

Acknowledgment

We are very thankful to the Principal of SMBT COLLEGE OF PHARMACY and SMBT Sevabhavi trust, Dhamangaon Nasik. Maharashtra India for providing facilities in our review.

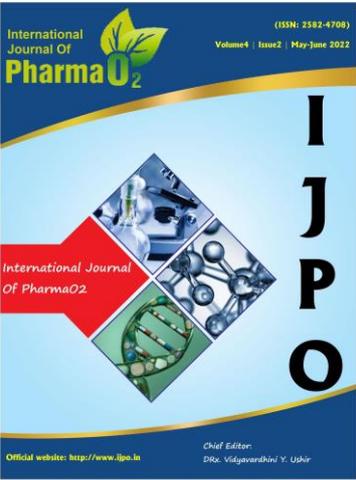
Special thanks to Dr. Yogesh .V. Ushir Sir ,Mr. Kundan Tiwari Sir & Mr. Dipak Suresh Throat.

References

1. Lemke TL, Williams DA, Roche VF, Foye's principles of medicinal chemistry, 6th edition Lippincott Williams and Wilkins. 2008, 175-200.
2. Block JH, Beale JM, Wilson and gisvold's textbook of organic medicinal and pharmaceutical chemistry, 11th edition, Lippincott Williams and Wilkins New York,`
3. SylvainMoriris, Drug Design, 1st edition, sarup book publishers pvt.ltd. New Delhi, 2009, 6- 40.
4. Gupta R.R., Kumar M., Heterocyclic chemistry-II, five-membered Heterocycles, 1st edition Springer, 2005, 1-2.
5. Rawat J, Jain PK, Agrawal RK, Synthesis and evaluation of mutual prodrugs of isoniazid, Paminosalicylic acid and ethambutol, ARKIVOC 2007(i):105-118.
6. Chaudhary S, Singh R. K, Synthesis and Biological Activity of Peptide Derivatives of 2- Hydroxy-5-(6-Iodo-2-methyl-4-oxoquinazolon-3(4H)-yl) Benzoic acid, Asian Journal of Pharmaceutical and Clinical research, 2012; 5(4):196-200.
7. Kim Kyoung-Ho, Kim Kong-Soo, et al, Effect of Dissolution Properties of P-Aminosalicylic acid with Chitin and Chitosan Mixtures, Publish by the Polymer society of korea, 1988;12(1):56-62.
8. Jensen K, Karl G, Tuberculostatic Derivatives of P-Aminobenzoic acid I. Esters and Amides of 4-Aminosalicylic Acid, research Laboratory of AB Ferrosan, Malmo, Sweden, ACTA CHEMICA SCANDINAVICA 1948;2:220-224.
9. Malipeddi H, Malipeddiven K, et al, Ultrasound-Mediated synthesis pyrazine-2- carboxylamino acid and

- Dipeptides as potent insecticides and anthelmic agents, IJRAP, 2010;1(1):180-185.
10. Abdurrahman J, Wahyunigrum D, et al., Synthesis of Dipeptide Benzoylalanyl glycine methyl Ester and Corrosion Inhibitor Evaluation by tafel equation, SainsMalaysiana2011;40(9):973-976.
 11. Patel PK, Patel PD, Metal Complexation studies of 1-(4-carboxy-3-hydroxy-4-phenyl amino methyl) benzotriazole, world wide web publications, E-journal of chemistry 2009;6(2):P:475-480.
 12. Shinde NV, Dhake AS, et al., Biological Activities of Cyclic Peptides: An Overview, Research Journal of Pharmaceutical, Biological and Chemical Sciences, 2013; 4:142-158.
 13. Richon AB, Young SS, An Introduction to QSAR Methodology, An Introduction to QSAR Methodology, 2008:1-33.
 14. Park J, Malinverni J, et al. Quantitative structure-activity relationship (QSAR) analysis of aromatic effector specificity in NtrC-like transcriptional activators from aromatic oxidizing bacteria, FEMS microbiology letters 2003;224:45-52.
 15. Patel PK., Patel PD., synthesis, characterization, metal complexation studies and biological screening of some newly synthesized metal complexes of 1-(4-carboxy-3-hydroxy-Nisopropyl phenyl amino methyl) benzotriazole with some transition metals, Chem. Tech research, 2010:2(2); 1147-52.
 16. Benerji B., Pramanik S., et al potent anticancer activity of cystine-based dipeptides and their interaction with serum albumins, chemistry centre journal, 2013;7; 1-10
 17. Reddy VS., Haripriya K., et al synthesis, characterization and anthelmintic activity of 4-(2- (5-nitro) imidazolyl) benzoyl (N-methyl) amino acid derivatives, IJPI, 2012:2(2); 45-60.
 18. Tsume Y., Bermejo B., et al the dipeptide monoester prodrugs of floxuridine and gemcitabine-feasibility of orally administrable nucleoside analogs, Pharmaceuticals, 2014:7; 168-180.
 19. Fattah MEA., Soliman AH., et al synthesis and biological activity of some new heterocyclic compounds, 2010; 1-5.
 20. Vicente E., Silanes S., et al selective activity against mycobacterium tuberculosis of new quinoxaline 1,4-di-N-oxides, Biological and medicinal chemistry, 2009:17; 385-389.
 21. Pandey R., Singh A., et al protein and peptide drug: a brief review, RJPT, 2009: 2(2); 228- 233.
 22. Chatwal G. R., "Organic chemistry of Natural products," Vol-I, Himalaya publishing house First edition 2006, 2.1-2.6.
 23. Patrick G. L., "An introduction to medicinal chemistry," second edition- 2003, OXFORD university press, 258-272, & 289-295.

24. P. Parimoo, A textbook of medicinal chemistry, first edition 2006, CBS publishers and distributors, Page no. 242-245.
25. Gary Hu, Understanding the fundamentals of peptides and proteins, Bioprocessing journal, Trends and Developments in Bioprocess technology, 10(1): 1-3.
26. Adki N, Kumar NS, et al, Synthesis of new biological active compounds containing linked thiazolyl-thiazolidineheterocycles, ACG publications, Org. commun. 2012: 5(4); 160-170.
27. Ansari KF, Lal C, synthesis and biological activity of some heterocyclic compounds containing benzimidazole and beta-lactam moiety, J. Chem. Sci. 2009: 121(6); 1017-1025.
28. Dutra LA, Melo TRF, et al Antitubercular drug discovery: the molecular modification as promise tool, international research of Pharmacy and Pharmacology, 2012: 2(1); 001-009.
29. Shinde VN, Himaja M, et al, synthesis and biological evaluation of analog of Delavaryin-C, a cyclic heptapeptide, Asian journal of chemistry, 2010: 22(2); 1-5.
30. Shinde Nirmala V, Himaja M, et al, synthesis and biological evaluation of delavaryin-C, Indian Journal of Pharmaceutical sciences, 2008: 70(6); 827-831.
31. Jack L. Strominger, M.D., et al, Bacterial Cell Wall Synthesis and Structure in Relation to the Mechanism of Action of Penicillins and Other Antibacterial Agents, American Journal of Medicine, 1965:39;1-14.
32. Virender K. Sarin, Stephen B. H. Kent, et al, Quantitative Monitoring of Solid-Phase Peptide Synthesis by the Ninhydrin Reaction', Analytical Biochemistry, 1981;117: 147-157. Jack L .Strominger, M.D . and Donald .I. Tipper, Bacterial Cell Wall Synthesis and Structure in Relation to the Mechanism of Action of Penicillins and Other Antibacterial Agents, AMERICAN JOURNAL OP MEDICINE, 1972;708-721



IJPO is

- Peer reviewed
- Bi-monthly
- Rapid publication
- Submit your next manuscript at