Review Article

Review on 6- Amino Penicillic Acid Compound and Their Applications

Wafa Abdel-Kazem Katie ,Ban Mahdi Salih, Muna Abass Hadi, Layla Ali Mohammed, Fatimah A. Wannas

Department Of Chemistry, College Of Education for Girls,U niversity of kufa ,Iraq

E-mail: *munaa.alsallami@uokufa.edu.iq*

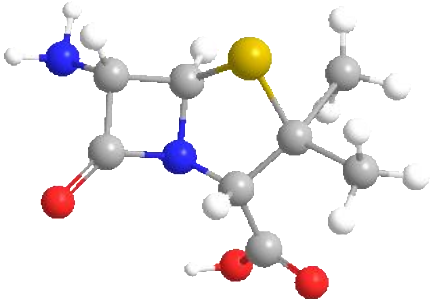
ABSTRACT

This review introduces 6- Amino Penicillic Acid (beta-lactam) which has great importance in the fields of pharmacy, Medicine, harmonics and organic chemistry. It plays a very important role for many Pharmaceutical compounds such as antibacterial and anti-tumor drugs. Attention has been drawn to this compound for its potential uses and applications in many fields. This preparation attempts to determine the importance of beta-lactam antibiotics (the commercially available antibiotics used are beta-lactams). Heterogeneous chemistry is also known, which is a branch of chemical reactions in synthetic chemistry that deals with the synthesis, properties, and applications of these heterogeneous rings.

Keywords: *6- Amino Penicillic Acid , heterocyclic compounds, biological activity of Beta lactam compounds .*

Introduction

6-Aminopenicillic acid is one of the compounds considered to be beta-lactam antibiotics, and its molecular formula is $C_8H_{12}N_2O_3S$ (3,3-dimethyl-7-oxo-4-thia-1-azobicyclo)-6-amino (S,5R, 6R2) and its molecular weight is (216.26 g/mol), as shown in the figure and has the structural formula as shown below:

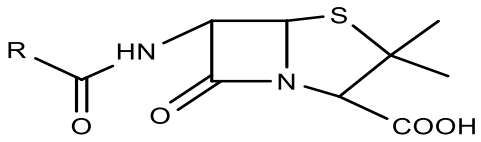


6-amino penicillic acid

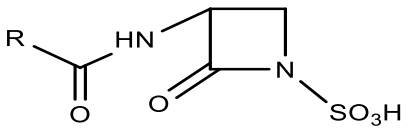
It was found that the compound that includes a beta-lactam ring in its composition is considered one of the penicillins, and 6-aminopenicillinic acid (6-APA) is also considered an important pharmaceutical intermediate for semi-synthetic penicillin drugs, which have taken up large areas in the production of cosmetics [(1)]. As an anti-inflammatory due to its "inhibitory" activity against pathogenic bacteria [(2)], its biological activity is attributed to the beta-lactam ring[(3)], which has important biological properties and interactions and is of great importance for changes within the body [(4)]. Work is still ongoing to explore this type of bio inhibitors from during the entry of these active and effective groups into the compounds and thus their contact with ionic minerals to form coordination compounds of biological importance.[(5)]. In the basic structure of 6-amino penicillic acid is linked to Five sites thiazolidine ring with a β-lactam ring containing four sites where it connects to side chain R-group [(6)].

Antibiotics that contain a quaternary beta-lactam that closes an amide bond. This type of antibiotic can be classified based on its chemical structure into: Penam (penicillin), Cephem, Clavam, Carbapenem, Monolactam(monobactams, nocardicins), each of these types has different uses, and most antibiotics derived from beta-lactam compounds are a two-ring system that may be a five- or six-ring ring. As for the monolactams type, it is distinguished by having a beta-lactam that is not linked to another ring, unlike the rest of the types[(7)].

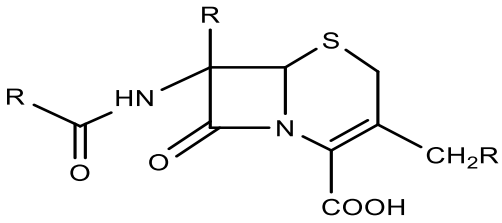
It is also classified depending on the chemical nature of the side chain attached to the beta-lactam ring, whether hydrophobic or hydrophilic[(8)]. As shown in the figures below:



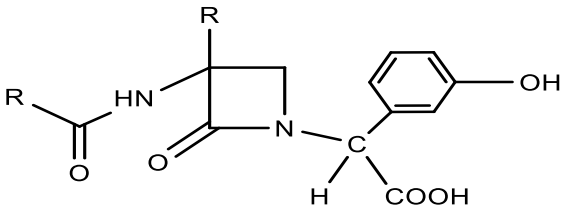
Penam



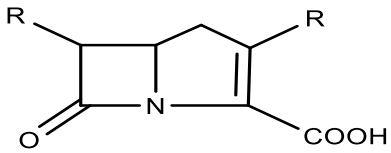
Monbactam



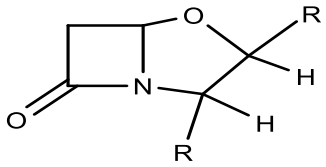
Cephem



Nocardicin



Carbapenem



Clavam

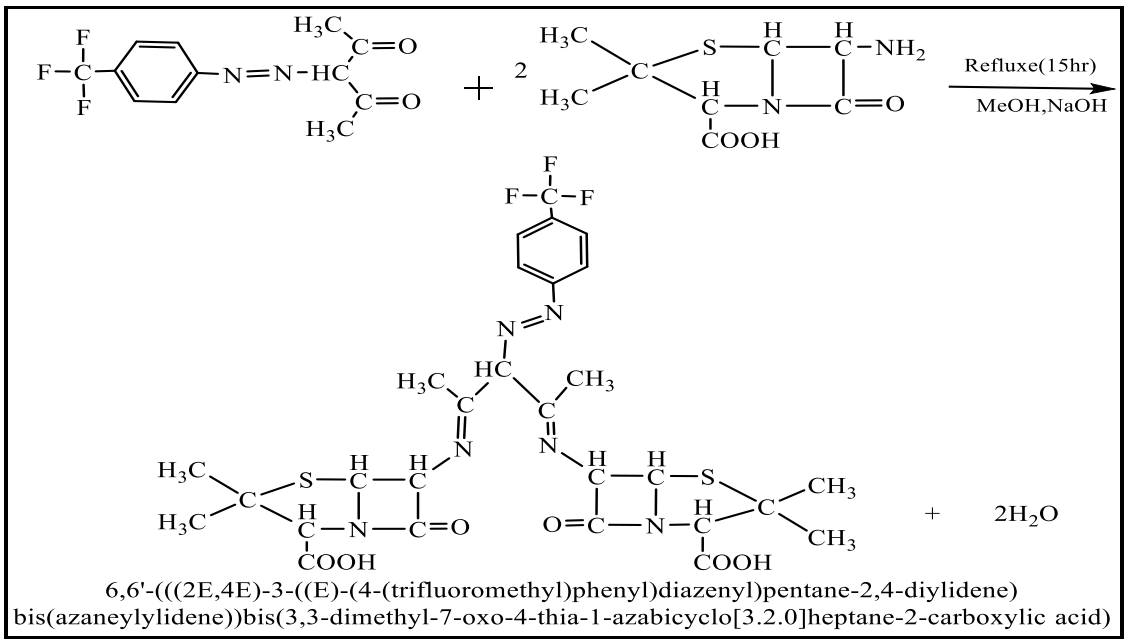
Penicillin is considered the most important of the classes of beta-lactam compounds and the first to be traded as an antibiotic. Penicillin includes its down classes, which include, Natural penicillin, Penicillinase-resistant penicillins, Amino penicillins, Extended spectrum penicillins, Amino penicillin/ beta lactamase inhibition combinations[9].

The meaning of "penam" is used to explain the common basic structure of one of the parts of penicillin. The beta-lactam ring is the main structural feature of penicillins and consists of four members. This structural part is essential for the antibacterial activity of penicillin [10]. The strained β-lactam ring causes the molecule to become non planar with a large angle and torsional rotation, which reduces the resonance of the amide bond and leads to stabilization of the β-lactam [11,12]. Several developments have led to compounds with favorable pharmacological and antimicrobial properties [13]. It acts as a broad-spectrum antibiotic due to its ability to inhibit protein synthesis in bacteria on ribosomes by causing misreading of the genetic code. [14].

Preparation of Azo and Azo-methine ligand from 6-amino penicillic acid compound:

Many organic compounds have been prepared from 6-amino penicillic acid, which has a major role as a biological activity in the medical and pharmaceutical fields.

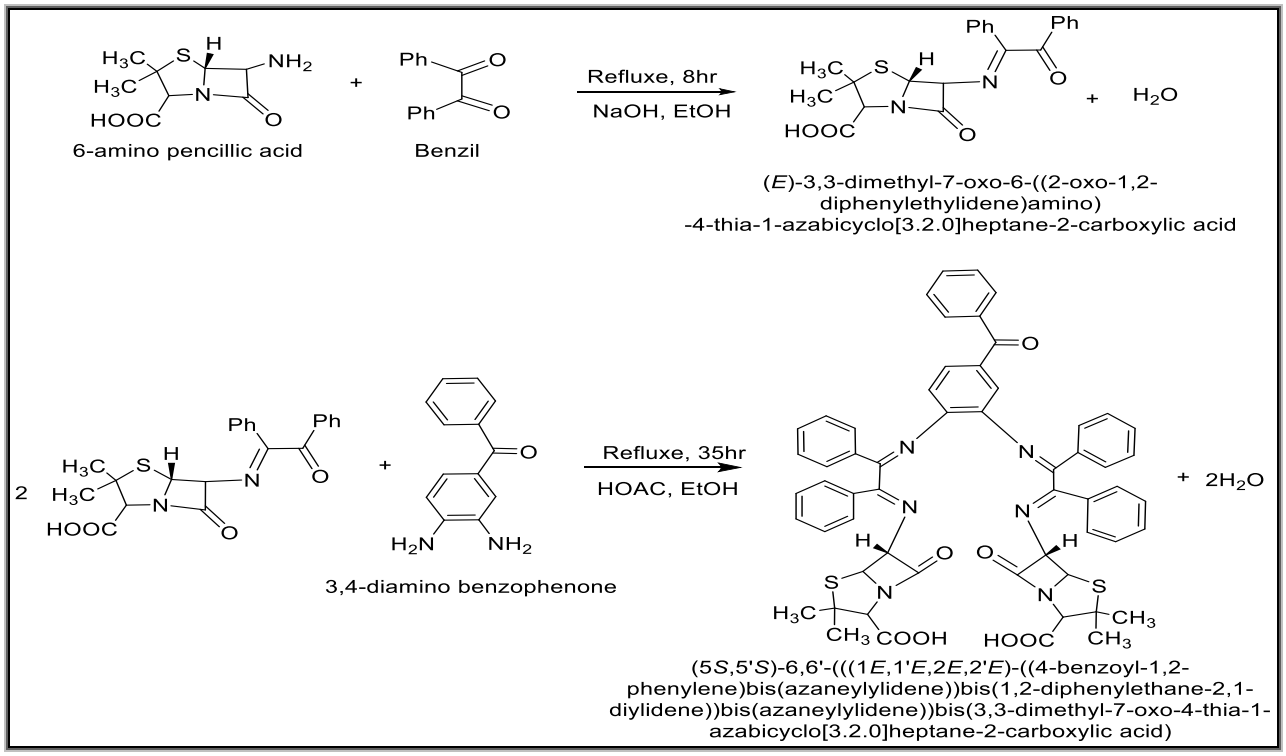
The researcher (Iman) [15] was able to prepare azo - Schiff base ligand derived from (6-APA), the preparation included two steps: The first step was to prepare the azo compound from the reaction of the compound (4-trifluoromethylaniline) with (acetyl acetone) to form the resulting azo compound. The second step included the method of condensation by reacting the azo compound with the compound (6-APA) in an alkaline medium, and it was characterization using available analytical methods, including TLC, UV-Visible, 1HNMR, Mass, CHN, and FT-IR to confirm this. Formation of the compound, followed by the preparation of a number of complexes for Co(II), Ni(II), Cu(II), Zn(II), Cd(II), Hg (II) and Au(III) The molar conductivity and magnetic sensitivity of these complexes were measured in addition to the aforementioned analytical methods to reach the proposed geometric shapes for these complexes. The biological activity of the gold complex $[AuL_4]Cl_3$ towards HT-29 colon cells, which is a model for infected cells, was also studied. The formula for the prepared ligand is shown in scheme below:



6,6'-(((2E,4E)-3-((E)-(4-(trifluoromethyl)phenyl)diazenyl)pentane-2,4-diylidene) bis(azaneylylidene))bis(3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid)

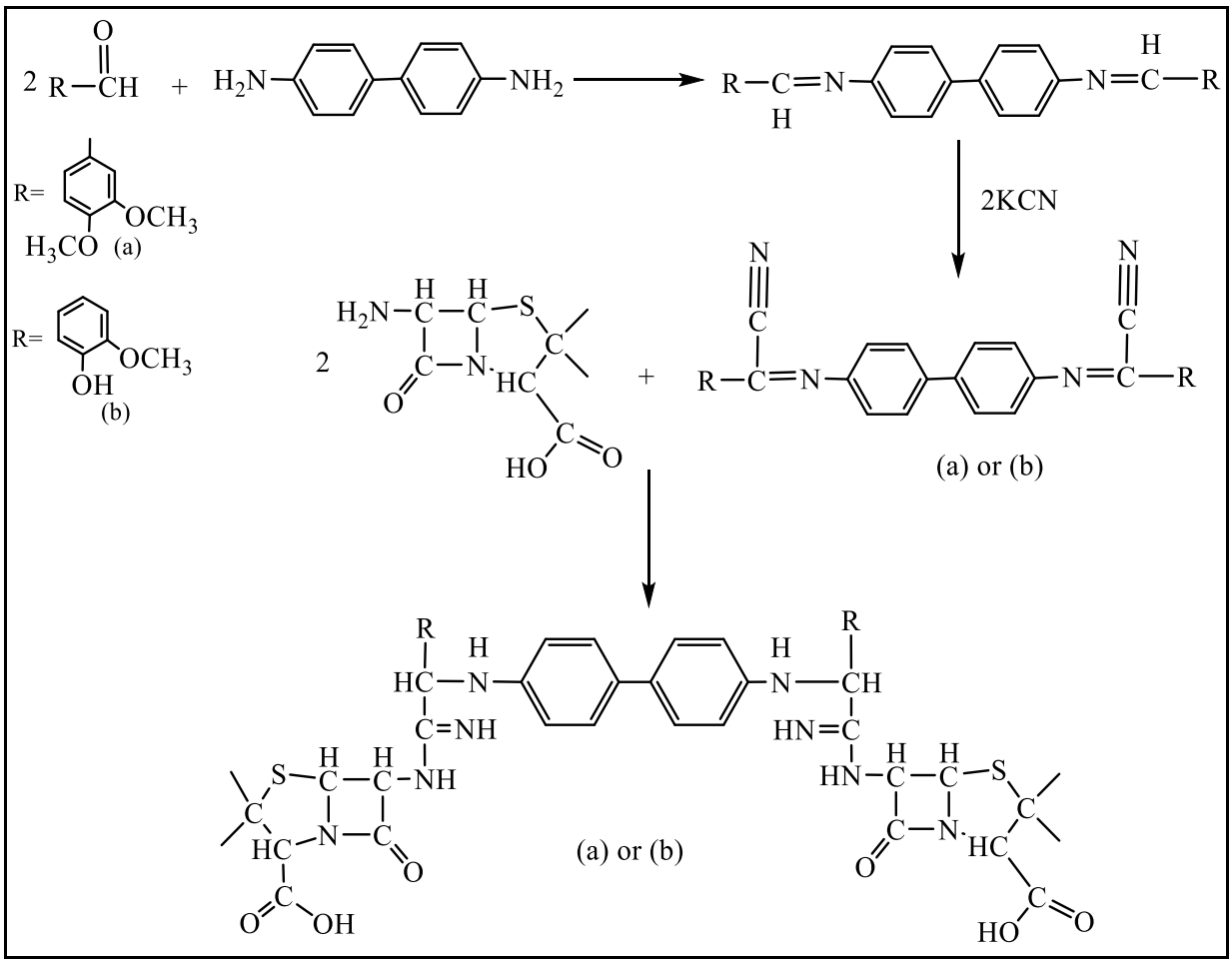
Scheme(1-1): Preparation of the azo-azomethine compound.

In study, researcher Muna [16] was able to prepare a tetra Schiff-base ligand (E)-2-(4-amino-1,5-dimethyl-1H-pyrazole-3(2H)-ylidinamino)-5-methylphenol(ADMPAM) in two steps. The first step included: the condensation method of 6-aminopenicillic acid with the benzyl compound, followed by the second step, which is the process of condensing the compound resulting from the first step with the 3,4-diaminobenzophenone compound. The prepared ligand was characterized through the various analytical methods available from it (Mass , 1HNMR, FT-IR, UV-Vis, CHN), after which many new solid metal complexes were prepared for this compound with different ions of the elements Co(II), Ni(II), Cu(II), Zn(II), Cd(II), Pt(II) and Au(III), and when studying the biological activity of this compound on the human colon and LS-174 colon cancer cells, the study showed that the compound $[AuL]Cl_3$ is characterized by high selectivity towards inhibiting cancer cells in addition to being very safe. Regarding normal cells taken from chimpanzees (kidney cells of the African green monkey), the schemes below shows the structural formula of the prepared ligand:



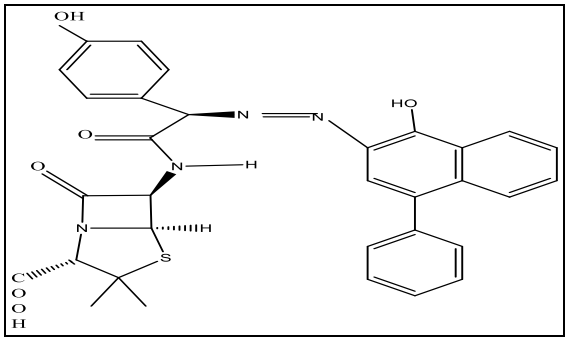
Scheme(1-2): Preparation of the Schiff base ligand from 6-APA

In other studies, researchers were able to conduct a new synthesis of two compounds derived from diamine through the reaction of (6-APA) with the compound (Di-alpha-amino nitrile) and two other derivatives referred to as (a, b). And (di-alpha-amino nitrile) for compounds (A and B) through the aldehyde and diamine condensation reaction in the presence of potassium cyanide in one vessel. The compound showed a "good" effect against selected bacteria [17]. The prepared compounds were characterized using different techniques, including (^{1}H-NMR) and (FT-IR) spectroscopy, and the following figure shows the method of preparing the two new compounds.

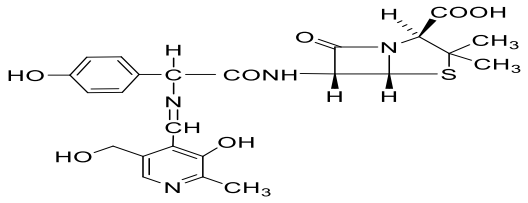


Scheme(1-3): preparation of the compounds derived from diamine.

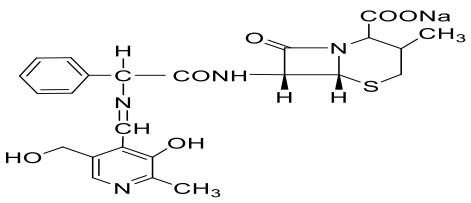
In her study, the researcher (Alaa) [18] was able to prepare a new azo ligand derived from a compound (6-amino penicillic acid), and the figure below shows that ligand:



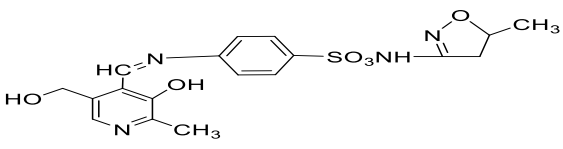
The researcher [19] Srivastava was able to prepare Schiff bases from the condensation of pyridoxyl with amine compounds such as (amoxicillin, ceplaxin, silfamethoxazole, triphoprim). The metal complexes of the Cu(II) ion were prepared. Suggesting the octahedral shape for all the complexes prepared after their identification by both spectroscopic and analytical methods, it is also characterized by its activity and high inhibitory ability against three types of bacteria (*P. aeruginosa*, *E-Coli*, *and S. aureus*). It was found that the inhibitory ability of the complexes is higher than that of the ligands when compared. The figures below show the structures of the prepared ligands.



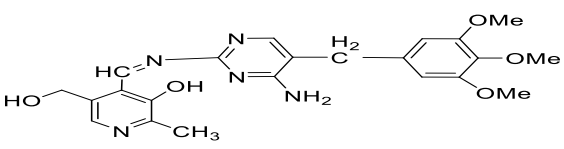
L_1H= Pyridoxylideneamoxicillin



L_2H= Pyeidoxylidenecephalexin



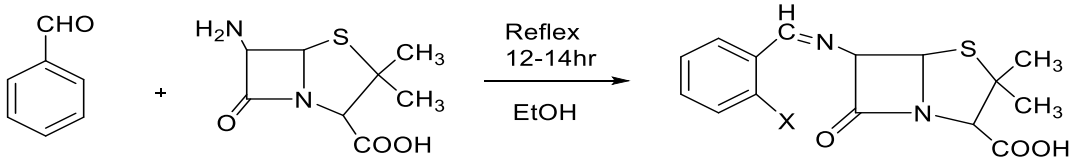
L_3H=Pyridoxylidenesulphamethoxazole



L_4H=Pyridoxylidenetrimethoprim

The researcher (Batool) [20] was able to prepare Schiff base ligands from the condensation of aldehyde with 6-APA compound, The metal complexes of the Cu(II)

, Co(II), Ni(II), Zn(II) ions were prepared. Suggesting the octahedral shape for all the complexes prepared after their identification by both spectroscopic and analytical methods, it is also characterized by its activity and high inhibitory ability against types of bacteria (*P. aeruginosa, S. faecalis P. mirabilis, and S. aureus*). It was found that the inhibitory ability of the complexes and ligands are higher. The formula for the prepared ligands is shown in scheme below.



X=H L1
X=OH L2
X=NO2 L3

Scheme(1-4): preparation of the compounds derived from(6-APA).

Penicillin biological activity

biological activity can be explained as substances produced by living organisms, which have the ability to inhibit the growth of living organisms in very low concentrations this is a more general definition. On the other hand, an antibiotic is a drug that inhibits the growth of bacteria. Antibiotics are one class of antimicrobials, and antimicrobials are a broad group that also includes antiviral, antifungal, and anti parasitic drugs [(21)].

The biological activity of penicillin is considered among the first drugs to have activity against many bacterial infections, and it is also considered among the most widely used and least toxic antibiotics. Studies have shown that about 10% of people suffer from an allergy to penicillin. However, more than 80% of this group may not be allergic to penicillin. Serious allergic reactions only occur in about 0.03% of people[(22)].

In 1928, researcher Alexander Fleming discovered penicillin, and it represented a broad development in medical and pharmaceutical sciences. Fleming also saw that molds (Penicillium species) have growth-inhibiting properties against a number of disease-causing bacteria[(23)]. After the discovery of penicillin, the mechanism by

which it inhibits cell growth was studied extensively. It has been found that penicillin and cephalosporin inhibit bacterial cell wall synthesis [(24)].

Antibiotics that contain beta-lactams in their composition are resistant to bacteria, as this resistance by bacteria is a complex function of the formation of beta-lactams enzymes, which is the ability of some bacteria to exclude these antibiotics from their cells and reduce the tendency for beta-lactams to bind to penicillin-binding proteins that they pass between cells. The action by which bacteria become resistant to β-lactams is due to the synthesis of β-lactamase enzymes that hydrolyze penicillins and cephalosporins before they can reach their receptors and the antibiotic cannot bind to the peptidoglycan layer [(25)].

Various methods have been discovered to deal with these factors. For example, increased stereo mass strategically placed near the side chain amide linkage often imparts greater stability against β-lactamases without significant loss of bioactivity[(26)].

Conclusion

In conclusion, it will be concluded that beta-lactam compounds derived from penicillin compounds and 6-aminopenicillic acid (6-APA) have a large and important role in biological activity, which is due to the presence of a beta-lactam ring. They have also been distinguished in the preparation of many organic compounds and metal complexes, and they also possess an important pharmaceutical intermediate. For semi-synthetic penicillin drugs. It also possessed high toxicity and selectivity towards inhibiting many types of cancer cells.

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