Myocardial infarction (MI) is a Cardiovascular state caused due to the blockage of arteries. The blockage is often, a result of a blood clot that is formed through platelet aggregation caused by thrombosis. There are different drugs used to treat this condition which possesses a thrombolytic activity. Alteplase and Tenecteplase are two such drugs used to treat MI and to remove blood clots. Both drugs are tissue plasminogen activators. The key difference between Alteplase and Tenecteplase is the mechanism of the production of the drug. Alteplase is produced by glycosylating a serine protease whereas tenecteplase is produced by complementary DNA (cDNA) modification of the tissue plasminogen activator by glycosylation at different bases.

What is Alteplase?

Alteplase is also known as Tissue plasminogen activator (TPA), is an approved drug by the Food and Drug Administration (FDA). Its molecular weight is around 70 kDa. Alteplase is a serine protease which is produced by modifying the protein by glycosylation. Alteplase has two main forms based on the number of chains it possesses; two-chain form and the one-chain form. It originally exists in the one chain form, but once exposed to fibrin it is converted to its dimer or the two-chain form.

The mechanism of its action is based on the property of fibrinolysis. Alteplase once administered, binds to the fibrin network of the clot and activates the plasminogen to produce more plasmin. Plasmin, in turn, has the capability of degrading the fibrin network. Thus, the clot or the thrombus formed is also degraded.

Binding of Alteplase to the fibrin takes place via the Kringle 2 domain and the finger-like domain of the fibronectin protein. Once the plasminogen is activated, the Alteplase is capable of cleaving the Arginine/Valine bond to degrade the plasminogen.
Alteplase is mainly used to clear blood clots during acute Myocardial infarction and other cardiovascular states. In addition, Alteplase is also used to clear blood clots in catheters. Alteplase is also exposed to allergic conditions and if it is taken in overdoses, the blood clotting process can be inhibited and may result in excessive bleeding.

**What is Tenecteplase?**

Tenecteplase is also a drug which acts as a tissue plasminogen activator and is approved by the FDA. The molecular weight of Tenecteplase is around 70kDa. The structure of Tenecteplase is rather complex. This genetically engineered protein drug is modified at several residues by glycosylation. Three amino acid substitutions during the recombination process can be identified.

1. Substitution of threonine 103 with Asparagine (Thr103Asn)
2. Kringle domain 1 - Substitution of Asparagine 117 with glutamine (Asn117Gln)
3. Protease domain – Tetra alanine substitution

Since these increase the polar nature of the protein, these modifications increase the ability of the drug to clear the plasma more easily and thereby increasing the stability of the drug. These modifications also increase the half-life of the drug. The main route of drug elimination can be done via the liver. Tenecteplase acts on the plasminogen and degrade the plasminogen to form plasmin, which in turn will start the thrombolytic activity of degrading the thrombus or the blood clot. Tenecteplase binds at the kringle 2 domain and cleave at the Arginine/valine bond to degrade plasminogen.

This drug is administered intravenously. It can produce side effects and lead to bleeding complications. Therefore, administering the accurate dosage is very important.

What are the Similarities Between Alteplase and Tenecteplase?

- Both act as tissue plasminogen activators and are involved in fibrinolysis
- Both drugs result in degrading the thrombus which is known as thrombolysis.
- Both drugs are proteases modified by glycosylation.
- Both drugs have a molecular weight closer to 70 kDa.
- Both drugs are administered intravenously.
- Both drugs bind at the kringle 2 domain of fibrin and cleave at the Arginine/Valine bond.
- Both drugs are excreted through the liver by the detoxification process.
- Both drugs may lead to complications and excessive bleeding if the wrong dosage is administered.

What is the Difference Between Alteplase and Tenecteplase?

<table>
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<tr>
<th>Alteplase vs Tenecteplase</th>
<th>Alteplase is a tissue plasminogen activator which is a glycosylated serine protease.</th>
<th>Tenecteplase is a tissue plasminogen which is modified via glycosylation at three instances resulting in amino acid substitutions.</th>
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<tr>
<td>Specificity to Fibrin</td>
<td>Alteplase has comparatively low specificity to fibrin than Tenecteplase.</td>
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Summary - Alteplase vs Tenecteplase

Both Alteplase and Tenecteplase are tissue plasminogen activators which bind to the fibrin network and activate plasminogen degradation. Thus, both drugs are proteases. Alteplase is modified by glycosylation and is a serine protease. Tenecteplase is modified at three levels by glycosylation. Both the drugs are involved in treating acute myocardial infarction and in clearing blood clots. Therefore, an excess of these drugs could lead to increased thrombolysis leading to excessive bleeding. Thus, care should be taken in administering the drug to patients with abnormal cardiovascular complications. This is the difference between Alteplase and Tenecteplase.

Reference:

2. “Tissue plasminogen activator.” Tissue plasminogen activator - an overview | ScienceDirect Topics. Available here

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