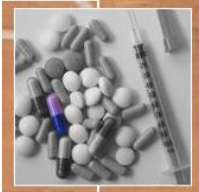
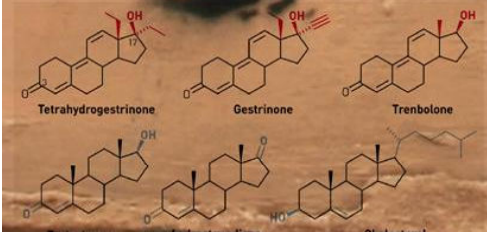
Tetrahydrogestrinone

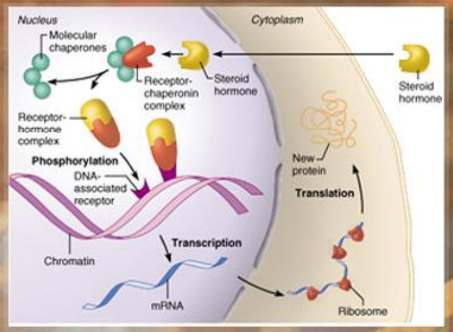
Tetrahydrogestrinone (THG) is a designer anabolic-androgenic synthetic steroid, that was only recently uncovered (2003). The drug was traced to the BALCO scandal in Los Angeles and was only uncovered due to the handing over of a syringe by an annoymous coach to the University of California, Los Angeles testing labs where anti-doping tests are performed on athletes. The difficulty indetecting stunned the world of sports.

THG (and anabolic drugs in general) encourages muscle hypertrophy (myoplasia) as well as myogenesis. It is androgenic in that it mimics testosterone, a naturally occuring male anabolic hormone and thus allows an athlete to train loger and harder without fatiguing.

THG was especially designed to evade "conventional" detection tecnhiques.







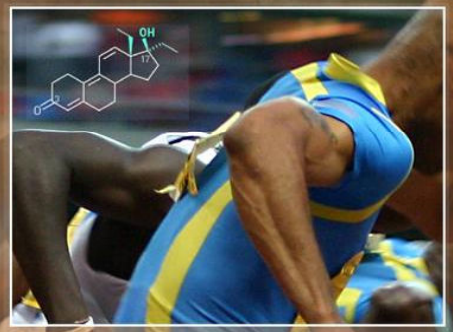
Mechanism of Action:

Briefly, steroids are classes of hormones that have cholesterol as a precursor. Being biochemically similar to cholesterol, the steroid is lipophilic, and thus most travel in the blood bound to plasma proteins. However, once the steroid hormone has reached its target cell, it can unbind from the plasma protein as the free steroids diffuse through the membrane of the target cell. It is generally accepted that steroid hormones induce the synthesis of new proteins by interacting with androgen & progesterone receptors within the cell – which are in fact transcription factors. (Note: androgen receptors, AR, share a similar biochemistry to progesterone receptors, PR as well as glucocorticoid receptors, GR)

More specifically, once the steroid (or androgen) binds to the androgen receptor in the cell cytoplasm (which exists as complexes with heat shock proteins), the receptor-steroid complex dimerilizes and then translocates into the nucleus if it is not already there, where binds to a hormone response element (HRE) and it summons co-activators and other transcription factors to form a pre-initiation complex. The better known co-activators of transcription include ARA70, ARA50 (androgen receptor activator) those of the p160 family. This then interacts with transcription machinery to trigger the transcription of select genes in the DNA of the cell nucleus which results in an mRNA that translates into a new protein. One gene the androgen receptor is known to target is the gene that codes for IGF-1 (Insulin-like Growth Factor 1). This might explain the mechanism behind how the steroid causes for cell growth via specific protein transcription.

This process takes quite sometime, unlike other hormones which have their end result mediated by secondary messenger G-proteins. Further, it has been seen recently that steroids have a DNA independent mechanism. Androgens have been shown to interact with certain signal transduction proteins in the cytoplasm which regulate DNA independent things such as ion fluctuation in and out of the cell. This could indirectly lead to alterations in transcription – for example, by leading to phosphorylation of other transcription factors.

Anabolic-androgenic steroids such as THG does not only affect muscle but many other tissues and so it is surprising that the vast range of biological actions could be the result of the steroid interacting with one molecular species androgen receptor with a singular mode of action; the transcriptional activation of elements in different genes. The exact mechanism by which anabolic-androgenic steroids mediate its actions on the body are at current unclear, but it is likely that there may involve other mechanisms independent of the generally accepted transcriptional activation of elements in the genes.



Advantages and Disadvantages:

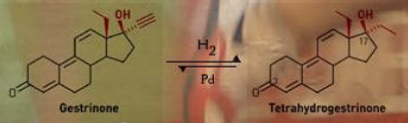
Being classed as an anabolic-androgenic steroid and having a molecular structure similar to testosterone and its other derivatives, we can assume that the general effects of THG would be similar to that of testosterone and result in the synthesis of new muscle protein; that is, muscle hypertrophy by myoplasia, myogenesis and thus have an effect on muscle power output amongst affecting many other tissues and organs. Other anabolic effects of androgens include accelerated bone growth, red blood cell production and enhanced neural conductions. Thus, THG has generally anabolic (or tissue building) effects.

Thus THG is advantageous in the following ways:

+ Builds up power and strength output
+ Builds up lean muscle mass and causes myoplasia & myogenesis
+ Increases body capacity to train and compete
+ Speeds up recovery time
+ Better utilization of ingested proteins
+ Increased retention of Nitrogen
+ Increases build - which some may find desireable
+ Used for atheletes whu require short burts of high energy output
  e.g: Sprinters, swimmers, rowers, gymnasts & weight-lifters

THG is disadvantageous in the following ways:

+ The drug must pass through the liver, being a poisonous substance, it may cause cirrhosis
+ May become addictive and result in withdrawal effects
+ Rise in cortisol may cause suppression of immune system



Molecular Structure:

THG is synthesized by the modification of one of gestrinone's functional groups. It part of the steroid family of biologically active chemcials, which means that is structurally similar to testosterone and has cholesterol as its precursor molecule. It is a lipid, thus hydrophilic, it is quickly eliminated in the blood if it does not travel bound to plasma proteins. It is made up of three 6-carbon rings and a single 5-carbon ring with the absence of the '19-nor'. By reacting gestrinone with hydrogen using a palladium catalyst, the alkyne at the 17a position is replaced by an alkane and THG is formed.

By modification of this single functional group, THG is a biologically active molecule that is very difficult to detect.

Techniques of Detection:

THG is a clear liquid that is orally administered, for this reason, THG is also known amongst athetes as 'the clear'. According to Dr Don Catlin, the doctor working at UCLA labs and discovered THG was especially designed to evade conventional testing techiques. It disentigrates when a urine sample is analysed and thus is undetectable in urine by standard anti-doping techniques. However, studies with a THG administered baboon does reveal that THG is excreted in the urine in trace amounts. THG is not produced endogenously in the body and cannot be taken unintentionally.

Today, Dr Catlin's lab in California, Los Angeles has developed new techniques to analyse urine and blood samples for the presence of THG. These techniques include the following:

+ Gas Chromatogrphy
  → Detects underivatized THG
+ High Resoultion Mass Spectrometry Analysis
  → Detects undervatized THG
+ Liquid Chromatography
  → Dectects the trimethylsilyl ether-oxime derivative
+ Tandem Mass Spectrometry
  → Dectects the trimethylsilyl ether-oxime derivative

Dr. Don Catlin © Ann Johansson