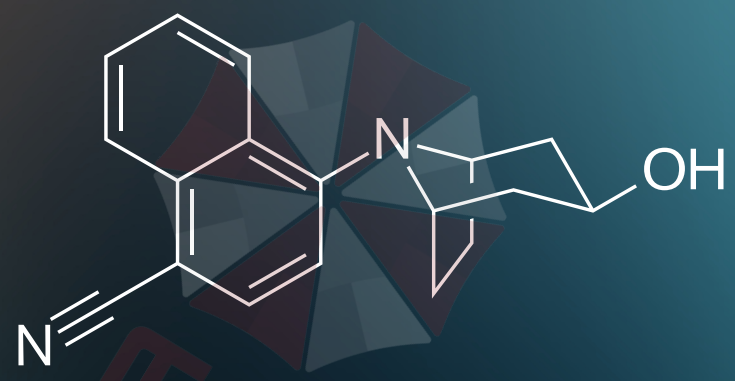

AC-262536 - A Selective Androgen Receptor Modulator with Potential Anabolic Benefits

AC-262 (also known as AC-262536) is part of the family of selective androgen receptor modulators (SARMs). This class has been proposed to be promising both for medical application but also for performance enhancement in athletes. Unlike classical steroids, SARMs have fewer side effects, but still retain anabolic activity. In addition, androgens are problematic to administer orally, because they suffer from a massive first-pass effect and damage the liver at the same time. SARMs have two main advantages: They usually do not have any hepatotoxic effects, but they also have fewer side effects connected their direct activation of androgen receptors (e.g. acne, prostate growth or hair loss/ growth in unwanted areas), because SARMs only activate specific subsets of the androgen receptor (like androgen receptors in skeletal muscle to promote growth). More specifically, they have the potential to increase muscle mass and performance, which is why SARM as tested to be used against Cachexia and age related muscle loss, without the problematic side effects of androgens like testosterone. In the case of AC-262, it was found to have stronger anabolic effects in muscle, but has a comparatively weak effect on prostate and seminal vesicle tissue. In that role and in chemical structure, it is very similar to the SARMs ACP-105, but also to vosilasarm, although the structural relationship is more distant in the later case.

Like other SARMs, AC-262 acts as a selective agonist of the androgen receptor (AR). AC-262 works as a partial agonist at the AR, meaning it activates the AR to a lesser extent than full agonists like testosterone, while still activating androgen receptor depended processes like muscle growth.

AC-262 was developed by Acadia Pharmaceuticals, first studies have been published in 2008.

Animal Studies

The first significant insights into AC-262's effects came from animal models. Studies conducted on castrated rats showed that AC-262 significantly increased muscle mass while reducing the size of androgen-sensitive tissues, particularly the prostate.

Preliminary characterization using indicated that AC-262 exhibits a slightly lower potency at the androgen receptor compared to the natural ligand testosterone (13 nM vs. 2 nM, respectively).[1] The same study also showed the partial agonistic behaviour of AC-262, given at 67 %

effect strength of testosterone. A potent selective non- steroidal AR agonist with partial agonism is particularly attractive, in regards to the potential for a wide separation between the anabolic and androgenic effects of androgens. As AC-262 displayed such properties, it was further evaluated in animal models of androgen actions.

Daily administration of testosterone to castrated rats for 14 days had a strong anabolic effect on the levator ani muscle, increasing its weight from 69 mg to 255 mg a 3.7-fold increase. AC-262 dose-dependently increased the size of levator ani to 192 mg at the highest dose of 30 mg/kg. At the 3 mg/kg dose, a partial but significant effect was evident compared to non-treated but castrated rats, reaching 23% relative to the effect seen with testosterone. At the 30 mg/kg dose, the effect achieved represented 66% of the maximum effect reached with testosterone. An ED50 of 17.3 mg/kg for AC-262 was calculated.

Treatment with testosterone over 14 days led to a 10-fold increase in the size of the prostate. In contrast, AC-262 had weaker effects on the prostate size. At 3 mg/kg, the size of prostate in castrated rats was not enlarged compared to control animals. At 10 and 30 mg/kg, the sizes of the prostates were similar: 55 mg and 54 mg, respectively. The androgenic effects of AC-262 on prostate thus reached a plateau at about 27 % of the maximum effects seen with testosterone. Similar results were achieved for seminal vesicles.

In prostate cancer cells, AC-262 was able to antagonize the effects of DHT, a strong natural androgen. The cancer cells react to DHT by multiplying and thus AC-262 was able to inhibit cancer growth in the presence of DHT.[1]

A metabolics study in horses has focused on the detection of AC-262 metabolites in order to set routines for doping control laboratories.[2] Urine, plasma and hair samples were collected and analyzed for parent drug and metabolites. Liquid chromatography-high-resolution mass spectrometry was used for in vitro metabolite identification and in urine and plasma samples. Nine metabolites were identified in vitro; four of these were subsequently detected in urine and three in plasma, alongside with unaltered AC-262. AC-262, but none of its metabolites was found to be stored in hairs as well. Another study with similar aim has focused specifically in the stability of AC-262 metabolites in urine.[3] The authors found the metabolites were stable for at least 1 year under ideal storage conditions.

A study has claimed that AC-262 specifically increases the production of androgen receptors in the brain, at least in female mice.[4] The authors put forward the idea, that this may be used to combat cognitive decline in elder humans. Typically, in seniors androgen levels in the brain are reduced, and application of a SARM such as AC- 262 may increase androgen signaling in the brain through increased receptor production.

Human Trials

There are no reports on trials involving humans with AC-262.

Conclusion

Given AC-262's properties as a SARM, AC-262 holds potential for a range of medical applications. One of the most promising uses is in treating conditions like sarcopenia (age-related muscle loss) and osteoporosis, where patients could benefit from increased muscle mass and bone density without the risks associated with traditional androgen therapy.

AC-262 does only have little data published about it. Critically, no studies on its toxicology and no human studies have been published so far. Hence, it is not clear of AC-262 is suitable for human use.

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