WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 6.805
Volume 5, Issue 9, 495-533. Review Article ISSN 2277– 7105

A BRIEF STUDY ON PERFORMANCE ENHANCING DRUGS (PED'S)

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Article Received on
11 July 2016,

Revised on 02 Aug. 2016,
Accepted on 23 Aug. 2016

DOI: 10.20959/wjpr20169-6970

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ABSTRACT

In present investigation, wedescribe the best Performance enhancing drugs now a day's used by the athletes, adults, children and physically weak patients for their physical improvements. These drugs are best for medicinal purpose but from ancient time these are also used by the athletes and by some adults who want to gain the desired physical fitness for various reasons. By studying these drugs we can get the knowledge about these drugs like what are their medicinal effects and what are the side effects of these drugs and how they are synthesized and what are their physical and chemical properties. By getting knowledge about these drugs we can improve and synthesize new PED's with less adverse effects.Besides this it envisages specific drug classes like stimulants,Narcotic analgesics, Anabolic-Androgenic steroids, Peptide Hormone, Diuretic, Creatine, Beta-2-Agonists etc., their unpleasant effects and structures.

KEYWORDS: PED's, Narcotic Analgesics, Stimulants, Peptide Hormone, Diuretic.

INTRODUCTION

The performance enhancing substances are also included inone of the type of drug. The use of performance enhancing drugs (PED's) by pre-teenagers and teenagers has increased tremendously over the past decade. This trend driven by multiple factors, including the decrease in the age of participation in competitive sports; the increase in the popularity of team/competitive sport; the focus of media on thinness of females; pressure from parents and coaches; the age-related characteristics of talking risks and feeling invincible; and availability PEDs many forms and shapes.

The use of performance enhancing drugs to enhance performance in sport has certainly occurred since time of the original Olympic games from [776 to 393 BC] The origin of the world 'doping' is attribute to Dutch word 'doop' which is a viscous opium juice, the drug of choice of ancient Greeks. The ancient Olympic champions were professionals who competed for huge cash prizes like olive wreaths. Most forms of what we would call cheating were perfectly acceptable to them, save for game fixing. There is evidence that they gorged themselves on meat – not a normal dietary staple of the Greeks – an experimented with herbal medicines in an effort to enhance their performances.[1]

Fig.1: Depiction of athletes competing at the ancient Olympic Games.

The first "effective" performance enhancing drugs, the amphetamines, which are widely used by soldiers in the Second World War, crossed over sports in early 1950s. These drugs – nicknamed la bomba by Italian cyclist and atoom by Dutch cyclists – minimize the uncomfortable sensations of fatigue during exercise.[5] From these facts of old time we can understand that the use of performance enhancing drugs is common from ancient time.These drugs were mainly invented during the Second World War for military purposes. In the WWII the army persons used Amphetamines to reduce their pain and don't get need some rest from their large hard work for long time.

Every two years as the Olympic Games begin, we hear about athletes using or, at least, being tested for performance-enhancing drugs. Sometimes, competitors raise the question when one athlete does particularly well. Other times, tests catch athletes with drugs in their systems. The practice of using artificial substances or methods to enhance athletic performance is called doping. Doping has become such a great concern that the United States formed the U.S. Anti-Doping Agency (USADA) in October 2000.

Athletes may have several reasons for using performance-enhancing drugs. An athlete may want to

- Build mass and strength of muscles and/or bones
- Increase delivery of oxygen to exercising tissues
- Mask pain
- Stimulate his or her body (increase alertness, reduce fatigue, increase aggressiveness)
- Relax
- Reduce weight
- Hide their use of other drugs

The pediatric clinicians must be aware of the use of performance enhancing substances by pediatric patients; be prepared to identify risk factors, signs, and symptoms; ask screening questions; and offer anticipatory guidance related to their use. There are many types of performance enhancing drugs according their use and effect but the main classification is :-

1. Stimulants: Drug that improves a person's energy level and alertness are called stimulants. These drugs help to improve and athlete's performance by stimulating the mental and physical functions that allow him to complete the longer periods without getting tired. Stimulants like caffeine or cocaine will improve your reaction times and make you more alert and confident. Side effect includes irritability, depression and aggression.

2. Narcotic analgesic: Narcotic analgesics (such as buprenorphine, morphine and heroin) are extremely potent painkillers that affect the nervous system. These drugs allow their users to train and complete without feeling pain from an injury. Narcotic analgesics can also help to relive anxiety levels before competitions. Side effect includes making your injury worse and they are also highly addictive and give bad withdrawal symptoms.

3. Anabolic and Androgenic steroid: Anabolic-androgenic steroids have the same chemical properties as testosterone (a male sex hormone). They help to improve muscle mass and help to reduce body's recovery time. There are two types of anabolic-androgenic steroids exogenous (the body can't produce naturally) and endogenous (the body can produce these naturally). Examples of exogenous and endogenous anabolic androgenic steroids include metenolone and androstenediol (or andro) respectively.

4. Peptide hormone: Different glands in the body produce peptide hormone that affect the performance of the other organs. Athletes take peptide hormones (such as corticotrophins, HGH and insulin) to improve strength and boost the red blood cell count. A high red blood cell count means that the blood can carry more oxygen, which helps improve performance.

5. Diuretics: These drugs will make you lose weight because you lose control your bladder sect and they decrease the amount of water in your body. Obviously this will mean you get dehydrated, nauseas, weak and dizzy. People in horse racing will use them so they don't weight as much and theirhorses can run faster.

6. Creatine: Creatine is the most popular supplement among the performance enhancing drugs in sport. It is sold over counter and is used to help the muscles release energy. Side effects of Creatine are stomach and muscle cramps, nausea, weight gain, and in high – doses liver and kidney damage.

7. Beta-2-Agonists: Beta to agonists dilates the muscles in the air passages by stimulating the beta cells. On inhaling, they produce the same effects as of stimulants while they can act as anabolic steroids when injected to body. Some of the most common beta 2 agonists are albuterol such as Accu Nab, Proventil HFA, ProAir HFA, Ventolin HFA, levalbuterol which includes Xeponex, Xeponex HFA and pirbuterol like Maxair, MaxairAutohaler etc. It is permissible for athletes suffering from breathing disorder to use inhalation – based beta 2 agonists to ward of bronchoconstriction during their performance.[2]

There are so many other types of performance enhancing drugs available which are not included in these types but have important effect in performance enhancement. Now days some researchers are doing work on those performance enhancing drugs which doesn't have any side effect but give the great result in the performance enhancement. Masking agents such as dextran and epitestesteron are prohibited for athletes as they make the detection of other prohibited drugs in the urine or the other samples impossible. Glucocortisteroids, including dexamethasone and prednisone, possess anti-inflammatory and pain reliving properties, which enable athletes to compete without even faintest sensation of pain. When injected directly into the blood, these drugs can also create a sense of ecstasy.

1. Stimulants: Stimulants (also called psycho stimulants) are psychoactive drugs which induce temporary improvements in either mental orphysical function or both. Examples of

these kinds of effects may include enhanced alertness, wakefulness, and locomotion, among others. Due to their effects typically having an "up" quality to them, stimulants are also occasionally referred to as "uppers". Depressants or "downers", which decrease mentaland/or physical function, are in stark contrast to stimulants and are considered to be their functional opposites. Stimulants are widely used throughout the world as prescription medicines and as performance enhancing drug substances of recreational use or abuse.

Stimulants (Analeptics) produce a variety of different kinds of effects by enhancing the activity of the central and peripheral nervous systems. Common effects, which vary depending on the substance in question, may include enhanced alertness, awareness, wakefulness, endurance, productivity and motivation, increased arousal, locomotion, heart rate and blood pressure, and the perception of a diminished requirement for food and sleep. Many stimulants are also capable of improving mood and relieving anxiety, and some can even induce feelings of euphoria.

Examples include cocaine, methamphetamine, amphetamine, methylphenidate, nicotine and MDMA (3, 4-methylenedioxymethamphetamine), better known as "Ecstasy".

Amphetamines: Adder all, an amphetamine mixture, is used by some college and high-school students as a study and test-taking aid. Amphetamine works by increasing energy levels, concentration, and motivation, thus allowing students to study for an extended period of time.[3-6]

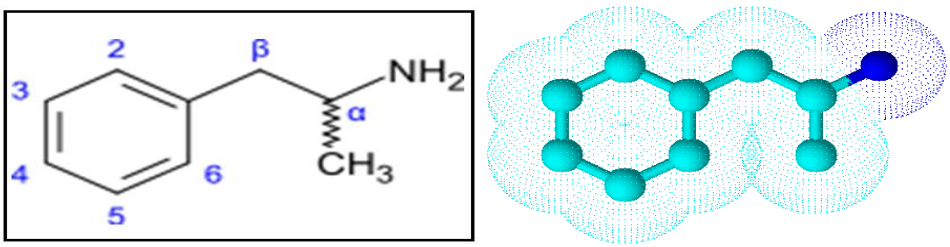


Fig.2: 1-phenylpropan-2-amine

Amphetamine was first synthesized in 1887 by Romanian chemist Lazer Edelenau and did not attract special attention. MDMA was first produced by in 1912 (according to other sources in 1914) as in intermediate product. However the synthesis also went largely unnoticed. In the 1920s, both methamphetamine and an optical isomer of amphetamine dextroamphetamine (D-Amphetamines) were synthesized. This synthesis was a by-product of a search for ephedrine a bronchodilator used to treat asthma, extracted exclusively from

natural sources. Over the counter use of amphetamines was initiated early in 1930s by pharmaceutical company Smith, Kline and French (now part of GlaxoSmithKline), as a medicine (Benzedrine) for colds and nasal congestion. Subsequently, amphetamine was used in the treatment of narcolepsy, obesity, hay fever, orthostatic hypotension, epilepsy, Parkinson's disease, alcoholism and migraine. The "reinforcing"effects of amphetamines were quickly discovered and misuse of amphetamines has been noted as far back as 1936.[7]

For amphetamine synthesis (by leuckart method), a mixture of P-2-P and formamide (sometimes in the presence of formic acid), or ammonium format, is heated until a condensation reaction results in intermediate product N-formylamphetamine. In the second step, N-formylamphetamine is hydrolyzed typically using hydrochloric acid. The reaction mixture is basified, isolated and (steam) distilled. In the final step, the product is precipitated out of the solution, typically as the sulfate salt. Amphetamine base is oily liquid with a characteristic "fishy-amine" odor.

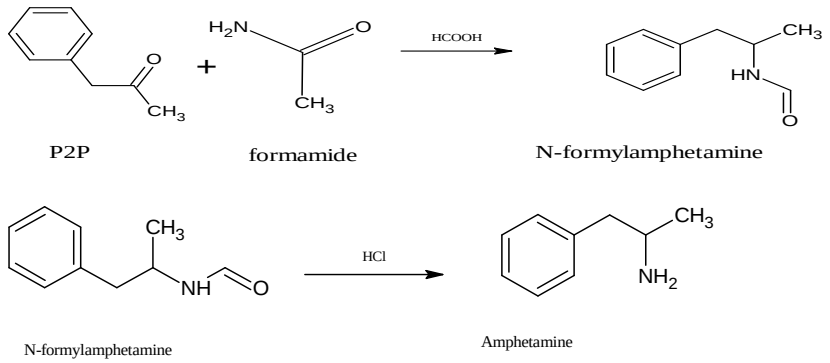


Fig.3: Synthesis of amphetamine by Leuckart method.

The Leuckart method is one of the most studied methods. Several route-specific impurities were identified and described in the literature. The most prominent impurities are the intermediate N-formylamphetamine (usually carried over into the final product) and 4-methyl-5-phenyl pyridine. Other synthetic routes do not give many route-specific impurities as the Leuckart method.

Amphetamine has been, and is still, used by militaries around the world. British troops used 72 million amphetamine tablets in the second world war[8-9] and the RAF used so many that "Methedrine"won the Battle of Britain" according to one report. American bomber pilots use amphetamine ("go pills") to stay awake during long missions. The Tarnak Farm incident, in which an American F-16 pilot killed several friendly Canadian soldiers on the ground, was

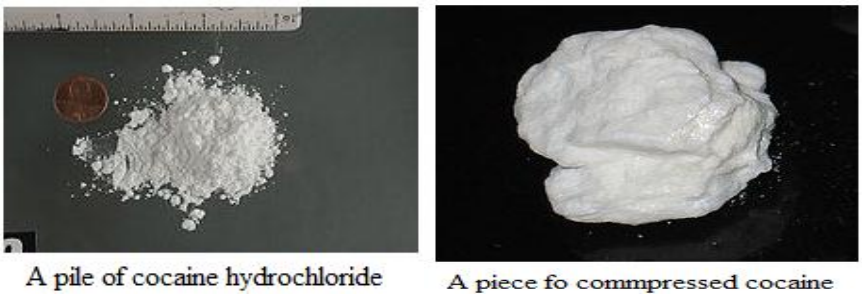
blamed by the pilot on his use of amphetamine.[10-11] A no judicial hearing rejected the pilot's claim.

Amphetamine is also used by some professional, collegiate and high schoolathletes for its strong stimulant effect. Energy levels are perceived to be dramatically increased and sustained, which is believed to allow for more vigorous and longer play. However, at least one study has found that this effect is not measurable. The use of amphetamine during strenuous physical activity can be extremely dangerous, especially when combined with alcohol, and athletes have died as a result, for example, British cyclist Tom Simpson.[12-15]

Amphetamine use has historically been especially common among Major League Baseball players and is usually known by the slang term "greenies".[16] In 2006, the MLB banned the use of amphetamine. The ban is enforced through periodic drug-testing. However, the MLB has received some criticism because the consequences for amphetamine use are dramatically less severe than for anabolic steroid use, with the first offense bringing only a warning and further testing.[17-19]

Amphetamine was formerly in widespread use by truck drivers to combat symptoms of somnolence and to increase their concentration during driving, especially in the decades prior to the signing by former president Ronald Reagan of Executive Order 12564, which initiated mandatory random drug testing of all truck drivers and employees of other DOT-regulated industries. Although implementation of the order on the trucking industry was kept to a gradual rate in consideration of its projected effects on the national economy, in the decades following the order, amphetamine and other drug abuse by truck drivers has since dropped drastically. (See also Truck driver – Implementation of drug detection).[20]

Cocaine: Cocaine comes in two forms. Powder cocaine is hydrochloric salt, made from the leaf of the coca plant. "Crack" is a smoke able form of cocaine that is processed with Ammonia and baking soda and water, and heated to remove hydrochloride.



A pile of cocaine hydrochloride A piece fo commpressed cocaine

Fig.4

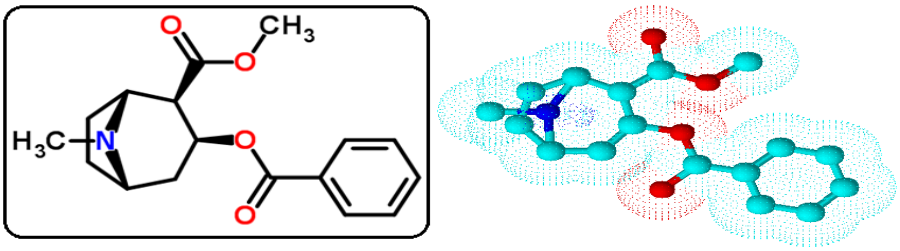


Fig.5: Methyl (3S, 4R)-3-benzoyloxy-8-azabicyclo [3.2.] octane-4-carboxylate

Cocaine was first was first prepared in 1923 by Willstatter et al (7). This synthesis is very remarkable because, although at this time both the relative and the absolute stereochemistry of cocaine were unknown, they were able to prepare this alkaloid in optically active form. Condensation of butane dial with methylamine and monomethyl acetonedicarboxylate 5 yielded methyl tropinone-2-carboxylate. Reduction of tropinone 6 with sodium amalgam produced a mixture of ecgonine methyl ester and pseudoecgonine methyl ester.[21]

The mixture of esters 7 and 8 was benzoylated with benzoyl anhydride, resulting in a mixture of cocaine[2] and pseudoecgonine[9], which was separated by fractional crystallization. The more soluble benzoate was *dl*-cocaine. Finally, *dl*-cocaine was resolved via the corresponding tartrate. Thus, crystallization with *l*-tartaric acid yielded the d-cocaine *l*-bitartrate, whose free base is natural *d*-cocaine (fig.6).

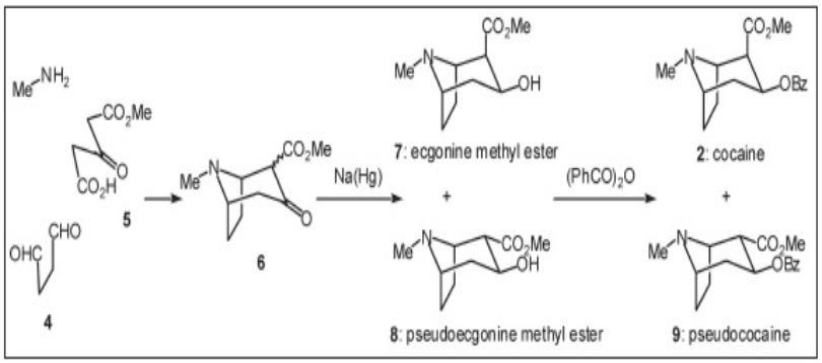


Fig.6

Cocaine isn't usually thought of as a performance enhancing drug the way steroid are, however, cocaine can enhance an athlete's performance in the short-term. Cocaine provides users with a sudden burst of energy and a surge of confidence and loss of inhibition. These effects can be attributable to a temporary improvement in performance on the field. Although it is not commonly heard of in sports today, many athletes have been busted for cocaine use in the past.[22]

Most laboratory-based studies have been limited by the low doses of cocaine that were allowed. At these single low doses, studies have shown performance enhancement in intentional abilities and increased behavioral and cortical arousal, but have no enhancement of effects on learning, memory, and other cognitive processes. Faster reaction times and diminished effects of fatigue have been observed. Improvements were greatest in behaviorally impaired subjects (e.g. sleep deprived, fatigued, or concurrent use of ethanol) and least improvements were observed in well-rested, healthy subjects. More deleterious effects are expected after higher doses, chronic ingestion and during drug withdrawal, and include agitation, anxiety, distress, inability to focus on divided attention tasks, inability to follow directions, confusion, hostility, time distortion, and poor balance and coordination. Laboratory studies have also demonstrated increased risk taking (rapid braking or steering) and deleterious effects on vision related to mydriasis. Self-reported increases in sensitivity to light, seeing halos around bright objects, flashes or movement of light in peripheral field, difficulty focusing, blurred vision, and glare recovery problems have been reported.[23-24]

2. Narcotic Analgesics

The term narcotic originally referred medically to any psychoactive compound with sleep-inducing properties. Narcotic analgesics are drugs that relieve pain, can cause numbness and induce a state of unconsciousness. They work by binding to opioid receptors, which are present in the central and peripheral nervous system. They work by binding to opioid receptors, which are present in the central and peripheral nervous system. There are three types of opioid receptors, which are all G-protein linked and either facilitate opening of potassium channels (causing hyper polarization) or inhibit calcium channel opening (so inhibits release of excitatory neurotransmitters such as substance P). Overall, narcotic analgesics reduce neuronal excitability in the pain carrying pathway.[25] Morphine and its analogues, and some synthetic derivatives are classed as narcotics analgesics. Narcotic analgesics are used to relieve acute and chronic, severe pain. Some narcotics are more potent than others. They also have the tendency to cause tolerance and dependence.[26]

Morphine: Morphine exerts a narcotic action manifested by analgesia, drowsiness, changes in mood, and mental clouding. The major medical action of morphine sought in the CNS is analgesia. Opiates suppress the "cough center" which is also located in the brainstem, the medulla. Such an action is thought to underlie the use of opiate narcotics as cough suppressants.[27]

Drugs belonging to this category can be studied under three broad categories

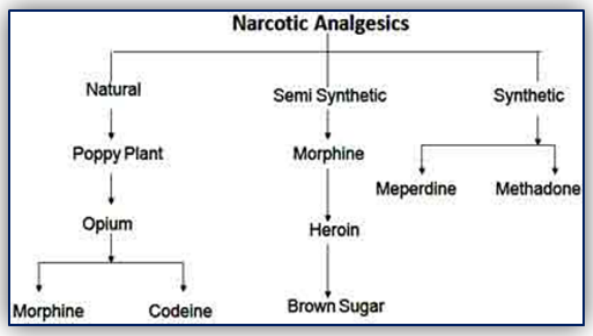


Fig.7

Morphine is principal alkaloid that is extracted from opium about 10 to 15 % of opium contains morphine. It is one of the most effective drugs for relief of pain. Morphine is the most abundant alkaloid found in opium, the dried latex extracted by shallowly slicing the unripe seedpods of the *Popover somniferous* poppy. Morphine was the first active principle purified from a plant source and is one of at least 50 alkaloids of several different types present in opium, poppy straw concentrate, and other poppy derivatives. Morphine is generally 8 to 14 percent of the dry weight of opium [28], although specially bred cultivars reach 26 percent or produce little morphine at all (under 1 percent, perhaps down to 0.04 percent). The latter varieties, including the 'Przemko' and 'Norman' cultivars of the opium poppy, are used to produce two other alkaloids, Theban and oripavine, which are used in the manufacture of semi-synthetic and synthetic opioid like oxycodone and etorphine and some other types of drugs. *P/bracteatm* does not contain morphine or codeine, or other narcotic phenanthrene-type, alkaloids. This species is rather a source of Theban.[29]

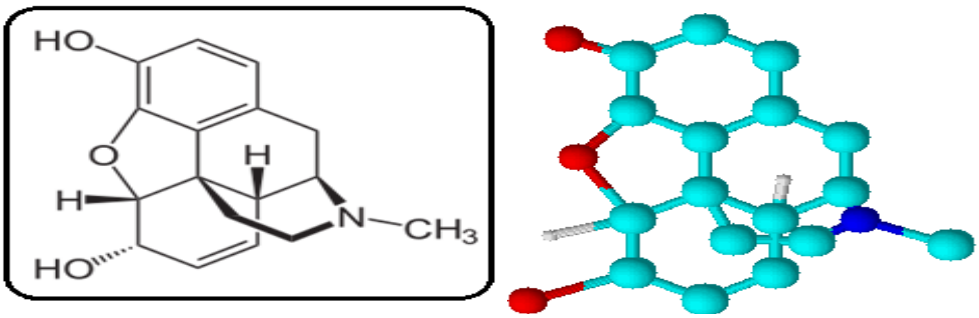


Fig.8: (5α,6α)-7,8-didehydro-4,5-epoxy-17-methylmorphinan-3,6-diol

Most reviews conclude that opioid produce minimal impairment of human performance on testsof sensory, motor, or attentional abilities. However, recent studies have been able to show some impairments caused by morphine, which is not surprising, given that morphine is a central nervous system depressant. In terms of cognitive abilities, one study has shown that morphine may have a negative impact on anterograde and retrograde memory [30-31], but these effects are minimal and are transient. One recent study analyzed COAT patients in order to determine whether they were able to safely operate a motor vehicle. The findings from this study suggest that stable opioid use does not significantly impair abilities inherent in driving (this includes physical, cognitive and perceptual skills). COAT patients showed rapid completion of tasks that require speed of responding for successful performance (e.g., Rey Complex Figure Test Rey Complex Figure Test) but made more errors than controls.[32]

Morphine is primarily used to treat both acute and chronic severe pain. It is also used for pain due to myocardial infarction and for labor pains.[33] There are however concerns that morphine may increase mortality in the setting of non ST elevation mycondralinfarction.[34] Morphine has also traditionally been used in the treatment of the acute pulmonary edema. A 2006 review however found little evidence to support this practice.[35] Immediate release morphine is beneficial in reducing the symptom of shortness of breath due to both cancer and non-cancer causes.[36-37] Its duration of analgesia is about 3–4 hours when administered via the intravenous, subcutaneous, or intramuscular route and 3–6 hours when given by mouth.[65] Morphine is also used in slow release formulations for opiate substitution therapy (OST) in Austria, Bulgaria, and Slovenia, for addicts who cannot tolerate the side effects of using either methadone or buprenorphine, or for addicts who are "not held" by buprenorphine or methadone. It is used for OST in many parts of Europe although on a limited basis.[38]

Heroin

Heroin (diacetylmorphine or morphine-diacetate (INN)), also knownasdiamorphine (BAN) and colloquially as smack, skag, horse, brown and other names is an opiate analgesicsynthesizedby C.R. Alder Wright in 1874 by adding two acetyl groups to the moleculemorphine found in the opium poppy. It is the 3,6-diacetyl ester of morphine, and functions as morphinepro-drug (meaning that it is metabolically converted to morphine inside the body in order for it to work).[39]

Heroin is synthesized from morphine by a relatively simple esterification reaction of two alcohol (phenol) groupswith acetic anhydride (equivalent to acetic acid). Heroin is much

more potent than morphine but without the respiratory depression effect. A possible reason may be that heroin passes the blood-brain barrier much more rapidly than morphine.

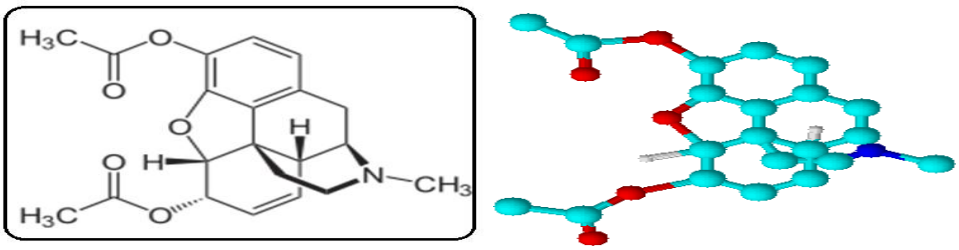


Fig.9: (5α, 6α)-7,8-didehydro-4,5-epoxy-17-methylmorphinan-3,6-diol diacetate

Under the chemical name diamorphine, diacetylmorphine is prescribed as astronganalgesic inthe United Kingdom, where it is given via subcutaneous, intramuscular, intrahecalor, intravenous route. Its use includes treatment for acute pain, such as in severe physical trauma, myocardial infarction, post-surgical pain, and chronic pain, including end-stage cancer and otherterminal illnesses. In other countries it is more common to use morphine or other strong opioid in these situations. In 2004, the National Institute for Health and Clinical Excellence produced guidance on the management of caesarian section, which recommended the use of intrahecalor or epidural diacetylmorphine for post-operative pain relief.[40]

Diacetylmorphine is also used as a maintenance drug to treat certain groups of addicts, normally long term chronic IV heroin users, and even in these situations it is only prescribed following exhaustive efforts at treatment via other means. It is thought that heroin users can walk into a clinic and walk out with a prescription but the process takes many weeks before a prescription for Diacetylmorphine is issued. Though this is somewhat controversial among proponents of a zero tolerance drug policy, it has proven superior to methadone in improving the social and health situation of addicts.[41-42]

A small percentage of heroin smokers, and occasionally IV users, may develop symptoms of toxic leuko encephalopathy. The cause has yet to be identified, but one speculation is that the disorder is caused by an uncommon adulterant that is only active when heated.[94, 95, 96] Symptoms include slurred speech and difficulty walking.[43-46]

Cocaine is sometimes used in combination with heroin, and is referred to as a speedball when injected or *moon-rocks* when smoked together. Cocaine acts as a stimulant, whereas heroin

acts as a depressant. Co-administration provides an intense rush of euphoria with a high that combines both effects of the drugs, while excluding the negative effects, such as anxiety and sedation. The effects of cocaine wear off far more quickly than heroin, thus if an overdose of heroin was used to compensate for cocaine, the end result is fatal respiratory depression.[47-50]

(a) Preparing heroin for injection

(b) Modified syringe for suppository administration

(c) one stamp of heroin

(d)Chunky"No.3" heroin

Fig.10: Heroin use in (a), (b), (c) and (d)

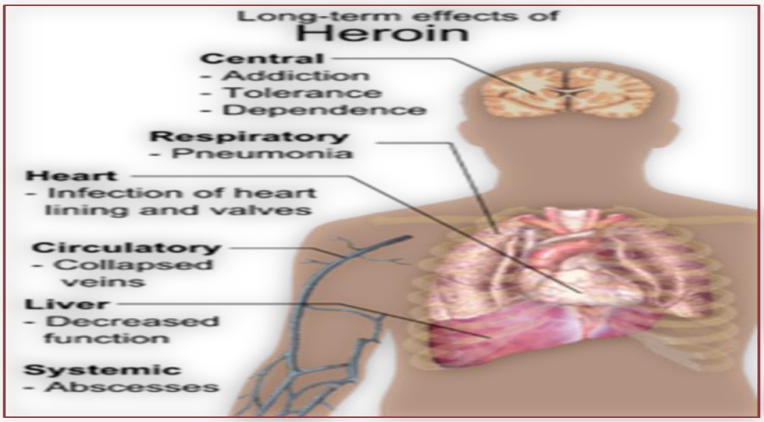


Fig.11: (a) Long-term effects of intravenous usage, including – and indeed primarily because of the effects of the contaminants common in illegal heroin and contaminated needles.

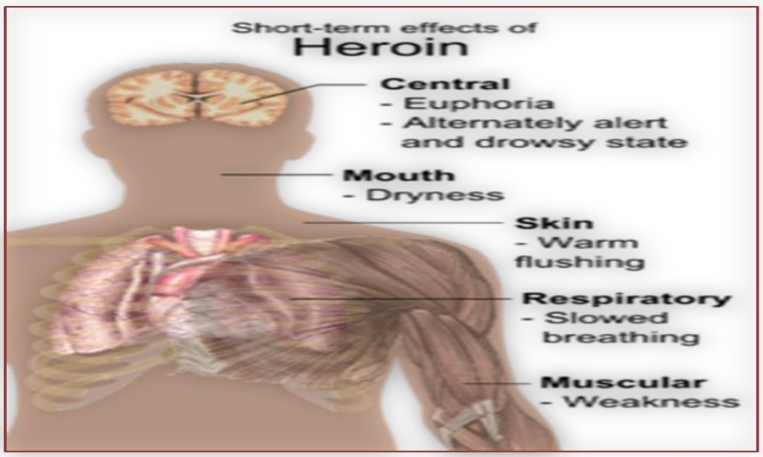


Fig.12: (b) short term effect of Heroin use

3. Anabolic-Androgenic Steroids (AAS)

Anabolic steroids, technically known as anabolic-androgenic steroids (AAS) or colloquially as "steroids", are drugs that mimic the effects of testosterone and dihydro-testosterone in the body. They increase protein synthesis within cells, which results in the buildup of cellulartissue(anabolism), especially in muscles. Anabolic steroids also have an drogenicandvirilizingproperties, including the development and maintenance of masculine characteristics such as the growth of the vocal cords, testicles, and body hair (secondary sexual characteristics).[51-52]

Anabolic steroids were first isolated, identified, and synthesized in the 1930s, and are now used therapeutically in medicine to stimulate bone growth and appetite, induce male puberty, and treat chronic wasting conditions, such as cancer and AIDS. AAS, in the presence of adequate diet, can contribute to increases in body weight, often as lean mass increases, and that the gains in muscular strength achieved through high-intensity exercise and proper diet can be additionally increased by the use of AAS in some individuals.[53]

Health risks can be produced by long-term use or excessive doses of anabolic steroids.[54-55] These effects include harmful changes in cholesterol levels (increased low-densitylipoproteinand decreased high-density lipoprotein), acne, high blood pressure, liver damage (mainly with oral steroids), and dangerous changes in the structure of the left ventricle of the heart. Conditions pertaining to hormonal imbalances such as gynecomastia and testicular atrophy may also be caused by anabolic steroids.[56]

Ergogenic uses for anabolic steroids in sports, racing, and bodybuilding are controversial because of their adverse effects and the potential to gain unfair advantage and considered cheating. Their use is referred to as doping and banned by all major sporting bodies. For many years, AAS have been by far the most detected doping substances in IOC-accredited laboratories.[57-58]

Testosterone: Testosterone (fig.13) is a steroid hormone from the androgen group and is found in mammals, reptiles[59], birds, [60] and other vertebrates. In mammals, testosterone is primarily secreted in the testicles of males and the ovaries of females, although small amounts are also secreted by the adrenal glands. It is the principal male sex hormone and an anabolic steroid.

In men, testosterone plays a key role in the development of male reproductive tissues such as the testis and prostate as well as promoting secondary sexual characteristics such as increased muscle, bone mass, and the growth of body hair.[61] In addition, testosterone is essential for health and well-being[62] as well as the prevention of osteoporosis.[63]

On average, in adult human males, the plasma concentration of testosterone is about 7-8 times as great as the concentration in adult human females' plasma[64], but as the metabolic consumption of testosterone in males is greater, the daily production is about 20 times greater in men.[65-66] Females also are more sensitive to the hormone.[67] Testosterone is observed in most vertebrates. Fish make a slightly different form called 11-ketotestosterone.[68] Its counterpart in insects is ecdysone.[69] These ubiquitous steroids suggest that sex hormone have an ancient evolutionary history.[70]

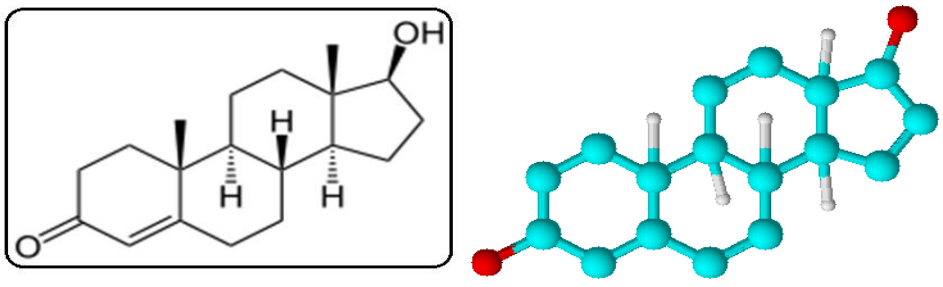


Fig.13: structure of Testosterone

Testosterone is derived from cholesterol(see fig.14).[71] The first step in thebiosynthesis involves the oxidative cleavage of the side chain of cholesterol by CYP11A, a mitochondrial Cytochrome P450 oxidase with the loss of six carbon atoms to give

pregnenolone. In the next step, two additional carbon atoms are removed bytheCYP17Aenzyme in the endoplasmic reticulum to yield a variety of C_{19} steroids.[72] In addition, the 3-hydroxyl group is oxidized by 3-β-HSD to produce androstenedione. In the final and rate limiting step, the C-17 keto group androstenedione is reduced by 17-β hydroxysteroid dehydrogenase to yield testosterone.

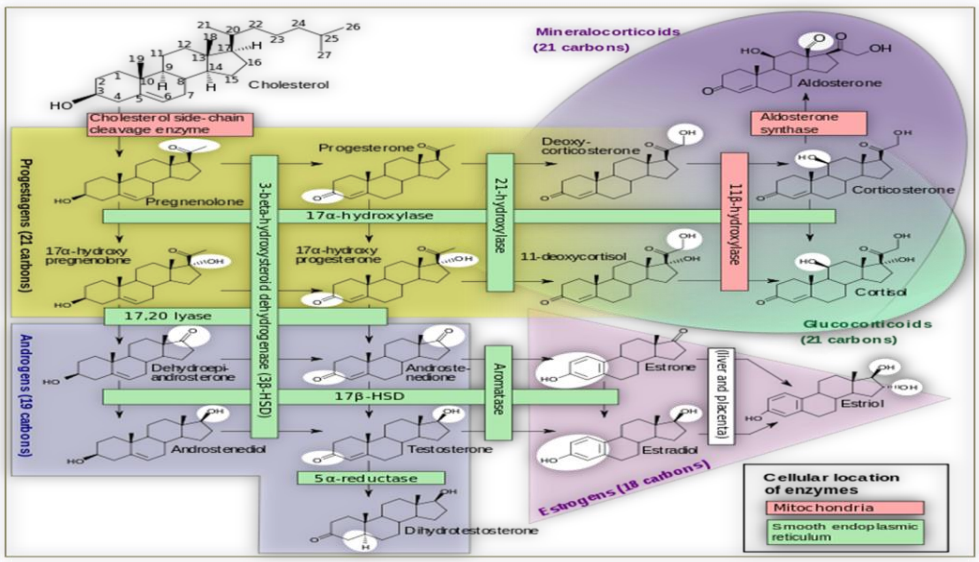


Fig.14: Synthesis of testosterone from cholesterol

The largest amounts of testosterone (>95%) are produced by the tests in men.It is also synthesized in far smaller quantities in women by the thecal cells of the ovaries, by the placenta, as well as by the zona reticularis of the adrenal cortex and even skin[73] in both sexes. In thetestes, testosterone is produced by the Leydig cells.[74] The male generative glands also containSertoli cells which require testosterone for spermatogenesis. Like most hormones, testosterone is supplied to target tissues in the blood where much of it is transported bound to a specific plasma protein, sex hormone binding globulin (SHBG).

Testosterone can be used by an athlete in order to improve performance, but it is considered to be a form of doping in most sports. There are several application methods for testosterone, including intramuscular injections, transdermal gels and patches, and implantable pellets. Supplement of the hormone results in lower metabolic production via the Farquharson phenomenon, creating long term dependence for improved performance level.

Anabolic steroids (including testosterone) have also been taken to enhance muscle development, strength, or endurance. They do so directly by increasing the muscles' protein

synthesis. As a result, muscle fibers become larger and repair faster than the average person's. After a series of scandals and publicity in the 1980s (such as Ben Johnson's improved performance at the 1988 Summer Olympics), prohibition of anabolic steroid use were renewed or strengthened by many sports organizations. Testosterone and other anabolic steroids were designated a "controlled substance" by the United States Congress in 1990, with the *Anabolic Steroid Control Act*.[75] The use is seen as being a seriously problematic issue in modern sport, particularly given the lengths to which athletes and professional laboratories go to in trying to conceal such abuse from sports regulators. Steroid abuse once again came into the spotlight recently as a result of the Chris Benoit double murder-suicide in 2007, and the media frenzy surrounding it – however, there has been no evidence indicating steroid use as a contributing factor.

4. Peptide Hormone

Peptide hormones are proteins that have endocrine functions in living animals.[76]

Like other proteins, peptide hormones are synthesized in cells from amino acids according to mRNA transcripts, which are synthesized from DNA templates inside the cell nucleus. Preprohormones, peptide hormone precursors, are then processed in several stages, typically in the endoplasmic reticulum, including removal of the N-terminal signal sequence and sometimes glycosylation, resulting in prohormones. The prohormones are then packaged into membrane-bound secretary vesicles, which can be secreted from the cell by exocytosis in response to specific stimuli (e.g.: an increase in Ca^{2+} and cAMP concentration in cytoplasm).[77]

These prohormones often contain superfluous amino acid residues that were needed to direct folding of the hormone molecule into its active configuration but have no function once the hormone folds. Specific endopeptidases in the cell cleave the prohormone just before it is released into the bloodstream, generating the mature hormone form of the molecule. Mature peptide hormones then travel through the blood to all of the cells of the body, where they interact with specific receptors on the surfaces of their target cells. Some peptide/protein hormones (angiotensin II, basic fibroblast growth factor-2, parathyroid hormone-related protein) also interact with intracellular receptors located in the cytoplasm or nucleus by an intracranial mechanism.[78]

Erythropoietin: Erythropoietin (fig.15), also known as erythropoetin or erthropoyetin or EPO, is a glycoprotein hormone that controls erythropoiesis, or red blood cell production. It

is a cytokine (protein signaling molecule) for erythrocyte (red blood cell) precursors in the bone marrow. Human EPO has a molecular weight of 34, 000.[79-80]

Also called hematopoietin or hemopoietin, it is produced by interstitial fibroblasts in the kidney in close association with peritubular capillary and tubular epithelial cells. It is also produced in perisinusoidal cells in the liver. While liver production predominates in the fetal and perinatal period, renal production is predominant during adulthood. Erythropoietin is the hormone that regulates red blood cell production. It also has other known biological functions. For example, erythropoietin plays an important role in the brain's response to neuronal injury.[81] EPO is also involved in the wound healing process.[82]

When exogenous EPO is used as a performance-enhancing drug, it is classified as an erythropoiesis-stimulating agent (ESA). Exogenous EPO can often be detected in blood, due to slight difference from the endogenous protein, for example in features of posttranslational modification.

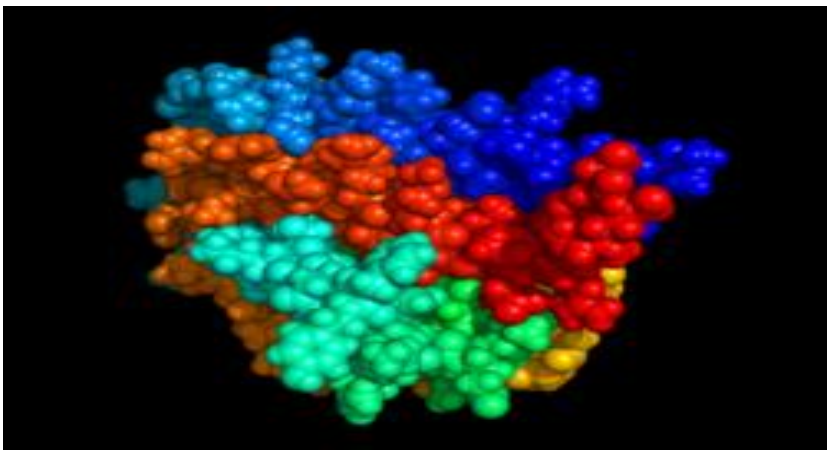


Fig.15: Erythropoietin

ESAs have a history of use as blood doping agents in endurance sports such as horseracing, boxing,[83]cycling, rowing, distance running, race walking, cross country skiing, biathlon, and triathlons. The overall oxygen delivery system (blood oxygen levels, as well as heart stroke volume, vascularization, and lung function) is one of the major limiting factors to muscles' ability to perform endurance exercise. Therefore, the primary reason athletes may use ESAs is to improve oxygen delivery to muscles, which directly improves their endurance capacity. ESAs increase hematocrit (% of blood volume that is red cell mass) and total red cell mass in the body, providing a good advantage in sports where such practice is banned.

EPO stimulates bone marrow to produce more red blood cells (RBC) and therefore hemoglobin. For this reason EPO is most commonly used amongst endurance athletes as a higher RBC count means better oxygen transportation and so a higher rate of aerobic respiration. The faster the rate of aerobic respiration, the higher the level at which the athlete can work without utilizing the anaerobic systems which produce lactic acid and cause fatigue.[84]

There are major side-effects of using erythropoietin which have proven to be fatal in previous cases

- Increased viscosity (thickness) of the blood (which increases the risk of heart attack and stroke)
- Fever
- Seizures (fits)
- Nausea
- Headache
- Anxiety
- Legarthy.

5. Diuretics: Diuretics, sometimes called water pills, help rid your body of salt (sodium) and water. They work by making your kidneys put more sodium into your urine. The sodium, in turn, takes water with it from your blood. That decreases the amount of fluid flowing through your blood vessels, which reduces pressure on the walls of your arteries.

Diuretics are used to treat heart failure, liver cirrhosis, hypertension and certain kidney disease. Some diuretics, such as acetazolamide, help to make the urine more alkaline and are helpful in increasing excretion of substances such as aspirin in cases of overdose or poisoning. Diuretics are often abused by sufferers of eating disorders, especially bulimics, in attempts at weight loss.[85]

The antihypertensive actions of some diuretics (thiazides and loop diuretics in particular) are independent of their diuretic effect. That is, the reduction in blood pressure is not due to decreased blood volume resulting from increased urine production, but occurs through other mechanisms and at lower doses than that required to produce diuresis.Indapamide was specifically designed with this in mind, and has a larger therapeutic window for hypertension (without pronounced diuresis) than most other diuretics.

Chlorothiazides: Chlorothiazide sodium (Diuril) is a diuretic used within the hospital setting or for personal use to manage excess fluid associated with congestive heart failure. It is also used as an antihypertensive.

Most often taken in pill form, it is usually taken orally once or twice a day. In the ICU setting, chlorothiazide is given to diurese a patient in addition to furosemide (Lasix). Working in a separate mechanism than furosemide, and absorbed enterically as a reconstituted suspension administered through a nasogastric tube (NG tube), the two drugs potentiate one another.Also known as:Diuril, Chlotride, Chlorothiazid, Chlorthiazide, Chlorosal, Chlortiazid, Chlorurit, Clotride, and Diuresal.[86]

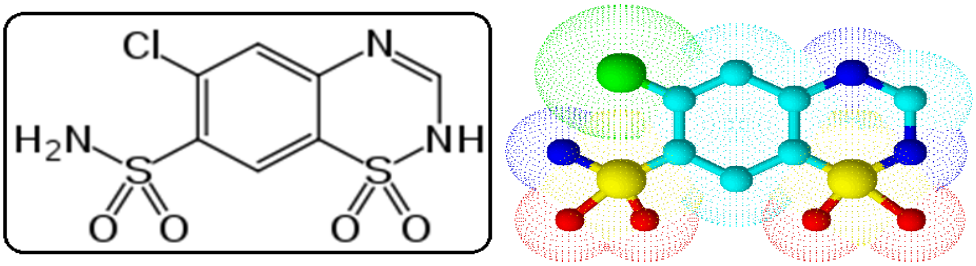


Fig.16: 6-chloro-1,1-dioxo-2*H*-1,2,4-benzothiadiazine-7-sulfonamide

Chlorothiazide, 1,1-dioxide 6-chloro-2*H*-1,2,4-benzothiadiazin-7-sulfonamide (3) is synthesized in the exact same manner, is all thiazide diuretics. 3-Chloroaniline (or 3-trifluoromethylaniline) undergoes sulfoylchlorination by chlorosulfonic acid, forming 4,6-sulfonochloride-3-chloroaniline (1) , the reaction of which with ammonia gives 4,6-sulfonylamido-3-chloroaniline (2) Heating this with formamide leads to formation of chlorothiazide (3).

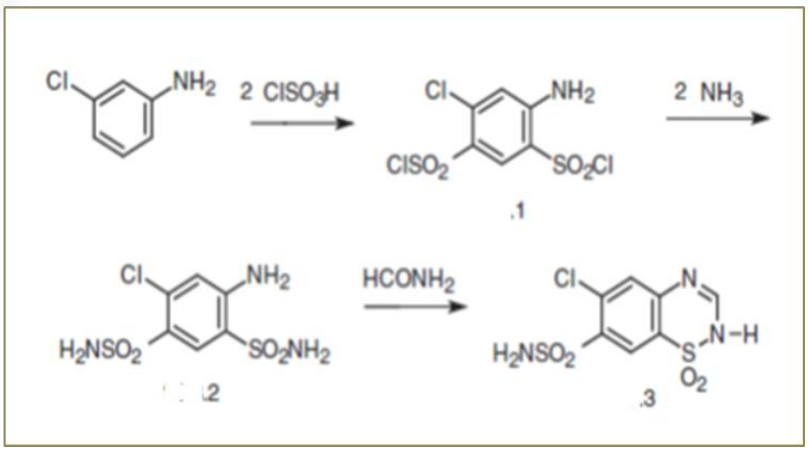


Fig.17: Reaction for the synthesis of chlorothiazide

The pharmacological actions of chlorothiazide are as Antihypertensive Agents: - Drugs used in the treatment of acute or chronic vascular HYPERTENSION regardless of pharmacological mechanism. Among the antihypertensive agents are DIURETICS; (especially DIURETICS, THIAZIDE); ADRENERGIC BETA-ANTAGONISTS; ADRENERGIC ALPHA-ANTAGONISTS; ANGIOTENSIN-CONVERTING ENZYME INHIBITORS; CALCIUM CHANNEL BLOCKERS; GANGLIONIC BLOCKERS; and VASODILATOR AGENTS.

Diuretics

Agents that promote the excretion of urine through their effects on kidney function. Sodium Chloride Symporter Inhibitors: Agents that inhibit SODIUM CHLORIDE SYMPORTERS. They act as DIURETICS. Excess use is associated with HYPOKALEMIA.

The diuretic action of chlorothiazide, like other drugs of this series, is caused by reduced absorption of sodium and chloride ions by the kidneys during their simultaneous, intense excretion from the organism. This drug exhibits strong diuretic action during both acidosis and alkalosis. It is used for arterial hypertension, in edematous syndromes of various genesis, congestive effects in cardiovascular insufficiency, nephrosis and nephritis, and toxicosis. It is especially recommended for hypertonic illnesses. It lowers intraocular pressure in a number of cases. Synonyms of this drug are clotride, diupres, diuril, and others.[87]

Metolazone

Metolazone is a thiazide-like diuretic marketed under the brand names Zytanix from ZydusCadila, Zaroxolyn, and Mykrox. It is primarily used to treat congestive heart faliureand high blood pressure. Metolazone indirectly decreases the amount of water reabsorbed into the bloodstream by the kidney, so that blood volume decreases and urine volume increases. This lowers blood pressure and prevents excess fluid accumulation in heart failure. Metolazone is sometimes used together with loop diuretics such as furosemide or bumetanide, but these highly effective combinations can lead to dehydration and electrolyte abnormalities.

Also known as

Zaroxolyn, Diulo, Microx, Mykrox, Metalozone, Metenix, Oldren, Metolazonum.

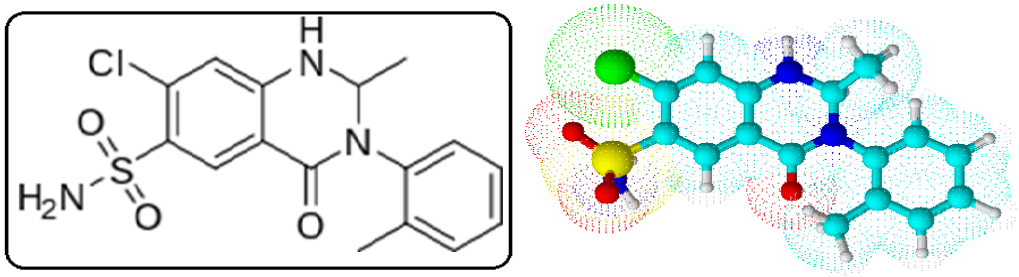


Fig.18: 7-chloro-2-methyl-3-(2-methylphenyl)-4-oxo-1, 2-dihydroquinazoline-6-sulfonamide

Metolazone, 7-chloro-1,2,3,4-tetrahydro-2-methyl-4-oxo-3-*o*-tolyl-6-quinazolinsulfonamide(9) is synthesized from 5-chloro-2-methylaniline. The amino group is acylated by ethyl chloroformate, forming 5-chloro-*N*-ethoxycarbonyl-2-methylaniline (4). The product, upon subsequent reaction with chlorosulfonic acid and ammonia, is transformed in the usual manner into 4-sulfonamido-5-chloro-*N*-ethoxycarbonyl-2-methylaniline (5). The methyl group of this product is oxidized by potassium permanganate, giving 5-sulfonamido-4-chloro-*N*-ethoxycarbonyl anthranylic acid (6). Upon treating this with thionyl chloride it cycles into the corresponding anhydride (7). This reacts with *o*-toluidine, turning it into 2-amino-5-aminosulfonyl-4-chloro-*o*-toluolbenzamide (8). Finally, reacting this with dimethylacetal acetic acid gives metolazone (9).[88](Fig. 19)

Metolazone acts on the distal tubules, thus increasing excretion of water and sodium,potassium, and chloride ions. It is used for treating edema caused by cardiac insufficiencyand adrenal irregularities, including nephrotic syndrome. Synonyms of this drug are diulo,matenix, and zaroxolyn.[89]

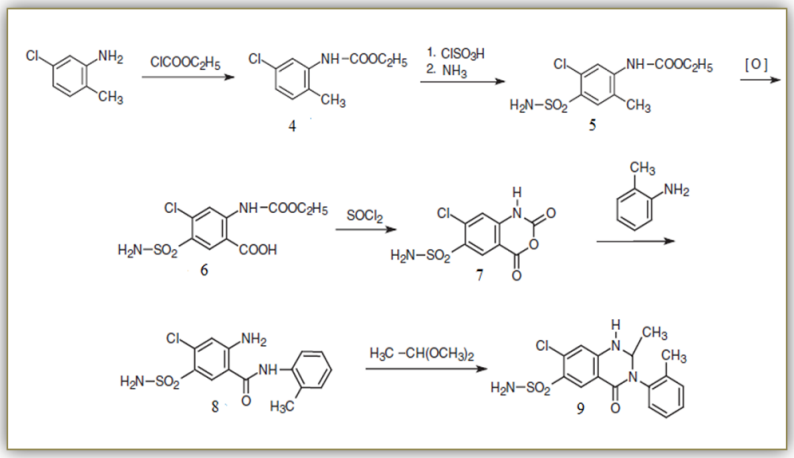


Fig.50: Reaction to synthesize metolazone

Metolazone may also be used in renal (kidney) disease, such as chronic renal failure or thenephrotic syndrome. Chronic renal failure causes excess fluid retention that is often treated with diet adjustments and diuretics.[91] Metolazone may be combined with other diuretics (typically loop diuretics) to treat diuretic resistance in CHF, chronic renal failure, and nephrotic syndrome.[92] Metolazone and a loop diuretic will synergistically enhance diuresis over the use of either agent alone. Using this combination, diuretic effects will occur at two different segments of the nephron, namely the loop diuretic will act at the loop of Henley, and metolazone will act at the distal convoluted tubule. Metolazone is frequently prescribed in addition to the loop diuretic. Metolazone may be used for edema caused by liver cirrhosis as well.

The other major use of metolazone is in treating hypertension (high blood pressure). Thiazide diuretics, though usually not metolazone, are very often used alone as first-line treatment for mild hypertension. They are also used in combination with other drugs for difficult-to-treat or more severe hypertension. "The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure" (JNC 7) recommends thiazide diuretics as the initial medication for treatment of hypertension. Hydrochlorothiazide is by far the most commonly used, as it is both better-studied and cheaper (about four times) than metolazone, although as mentioned above metolazone is used in patients with moderate renal failure.[90]

6. Creatine

Creatine is a nitrogenous organic acid that occurs naturally in vertebrates and helps to supply energy to all cells in the body, primarily muscle. This is achieved by increasing the formation of adenosine triphosphate (ATP). Creatine was identified in 1832 when Michel Eugene Chevreul discovered it as a component of skeletal muscle, which he later named after the Greek word for meat, *kreas*. In solution, creatine is in equilibrium with creatinine.[93]

Creatine is a naturally occurring amino acid (protein building block) that's found in meat and fish, and also made by the human body in the liver, kidneys, and pancreas. It is converted into creatine phosphate or phosphocreatine and stored in the muscles, where it is used for energy. During high-intensity, short-duration exercise, such as lifting weights or sprinting, phosphocreatine is converted into ATP, a major source of energy within the human body.

Also known as

Creatin, Kreatin, Krebiozon, N-amidinosarcosine, N-methyl-N-guanylglycine, Creatine, hydrate, (alpha-Methylguanido)acetic acid, Pyrolysate.

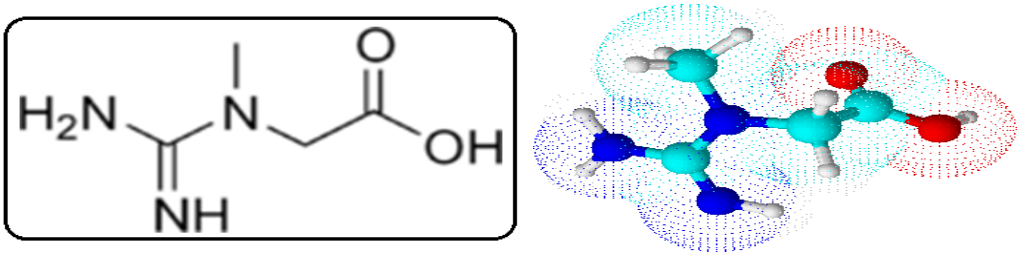


Fig.20: 2-[carbamidoyl(methyl)amino]acetic acid]

Creatine is naturally produced in the human body from amino acids primarily in the kidney and liver. It is transported in the blood for use by muscles. Approximately 95% of the human body's total creatine is located in skeletal muscle.[94] Creatine is not an essential nutrient, as it is manufactured in the human body from L-arginine, glycine, and L-methionine.

In humans and animals, approximately half of stored creatine originates from food (about 1 g/day, mainly from meat). A study, involving 18 vegetarians and 24 non-vegetarians, on the effect of creatine in vegetarians showed that total creatine was significantly lower than in non-vegetarians. Since vegetables do not represent the primary source of creatine, vegetarians can be expected to show lower levels of directly derived muscle creatine. However, the subjects happened to show the same levels after using supplements. Given the fact that creatine can be synthesized from the above mentioned amino acids, protein sources rich in these amino acids can be expected to provide adequate capability of native biosynthesis in the human body.[95-96]

The enzyme GATM (L-argineglycineamidinotransferase (AGAT), EC 2.1.4.1) is a mitochondrial enzyme responsible for catalyzing the first rate-limiting step of creatine biosynthesis, and is primarily expressed in the kidneys and pancreas.The second enzyme in the pathway (GAMT, Guanidinoacetate N-methyltransferase, EC:2.1.1.2) is primarily expressed in the liver and pancreas. Genetic deficiencies in the creatine biosynthetic pathway lead to various severe neurological defects.[97-98]

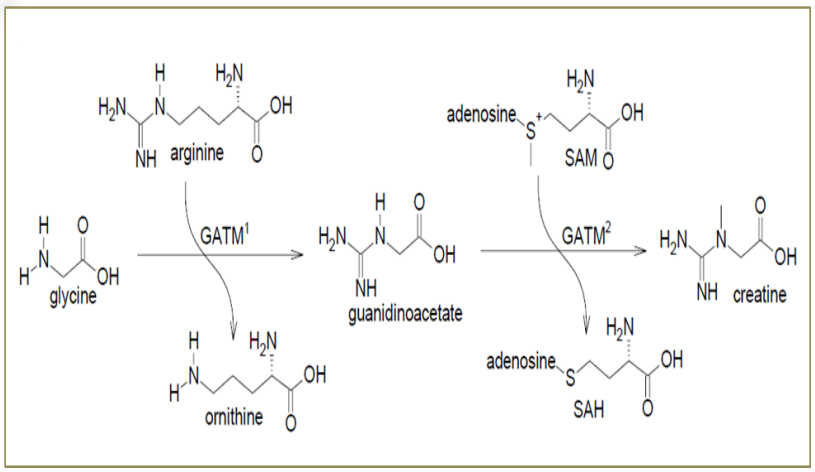


Fig.21: The pathway for the synthesis of creatine

Most human studies have taken place in laboratories, not in people actually playing sports. Although not all clinical studies agree, some conducted in both animals and people have shown that creatine supplements improve strength and lean muscle mass during high-intensity, short-duration exercises, such as weight lifting. In these studies, the positive results were seen mainly in young people, about 20 years old.

Creatine does not seem to improve performance in exercises that requires endurance, like running, or in exercise that isn't repeated, although study results are mixed. Although creatine is not banned by the National Collegiate Athletic Association (NCAA) or the International Olympic Committee, using it for athletic performance is controversial. The NCAA prohibits member schools from giving creatine and other muscle building supplements to athletes, although it doesn't ban athletes from using it.Creatine appears to be generally safe, although when it is taken at high doses there is the potential for serious side effects, such as kidney damage. High doses may also stop the body from making its own creatine. Some creatine supplements may be marketed directly to teens, claiming to help them change their bodies without exercising. One survey conducted with college students found that teen athletes frequently exceed the recommended loading and maintenance doses of creatine. But creatine has not been tested to see whether it is safe or effective in those under 19.[99]

7. Beta-2-Agonists

Beta2-agonists (bronchodilators) are a group of drugs prescribed to treat asthma.Short-acting beta-agonists (SABAs) provide quick relief of asthma symptoms. They can also be prescribed to be taken before exercising in order to prevent exercise-induced bronchoconstriction. Short-acting beta-agonists should not be used more than twice a week for shortness of breath.

Taking them more often is a sign of poorly controlled asthma. This means you should visit your allergist / immunologist to have your prescription adjusted.Examples of these short-acting medications include: albuterol (AccuNeb, Proventil HFA, ProAir HFA, and Ventolin HFA); levalbuterol (Xopenex, Xopenex HFA) and pirbuterol(Maxair, MaxairAutohaler).Long-acting beta-agonists (LABAs) are taken on a daily basis to relax the muscles lining the airways that carry air to the lungs. This allows the tubes to remain open, making breathing easier. LABAs should be taken only in combination with a corticosteroid to treat asthma. They are used in a metered-dose or dry powder inhaler.

Combinations of a long-acting beta2-agonist and inhaled corticosteroid include formoterol and budesonide (Symbicort), formoterol and mometasone (Dulera), and salmeterol and fluticasone (Advair).[100]

Salbutamol

Salbutamol (INN) or albuterol (USAN) is a short-acting β_2-adrenergic receptor agonist used for the relief of bronchospasm in conditions such as asthma and chronic obstructive pulmonary disease. It is marketed as Ventolin among other brand names.

Salbutamol was the first selective β_2-receptor agonist to be marketed — in 1968. It was first sold by Allen &Hanburys under the brand name Ventolin. The drug was an instant success, and has been used for the treatment of asthma ever since.[101]

Salbutamol sulfate is usually given by the inhaled route for direct effect on bronchial smooth muscle. This is usually achieved through a metered dose inhaler (MDI), nebulizer or other proprietary delivery devices (e.g. Rotahaler or Autohaler). In these forms of delivery, the maximal effect of salbutamol can take place within five to 20 minutes of dosing, though some relief is immediately seen. It can also be given orally, as an inhalant, or intravenously.

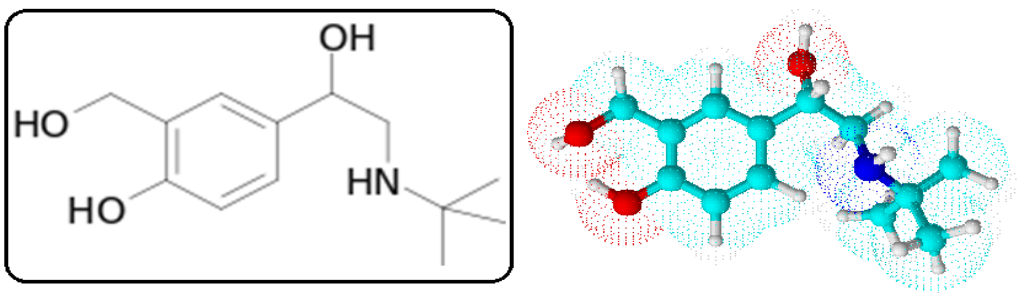
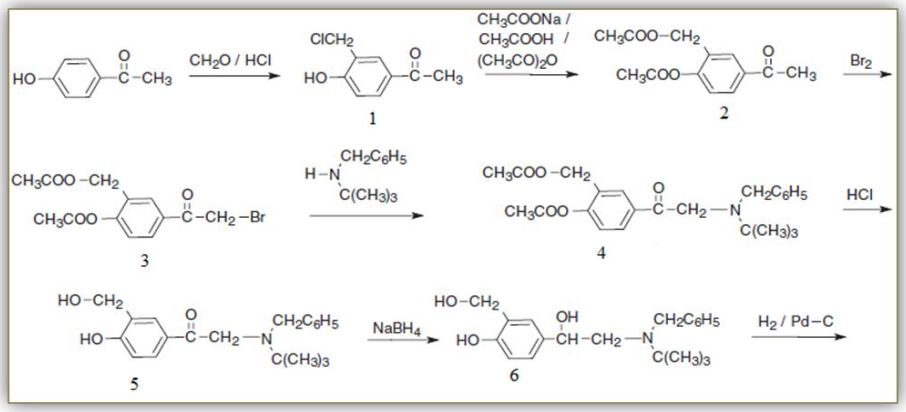


Fig.22: 4-[2-(tert-butylamino)-1-hydroxyethyl]-2-(hydroxymethyl) phenol]

Synthesis of Albuterol/Salbuterol:- 2-*tert*-butylamino-1-(4-hydroxy-3-hydroxymethylphenyl) ethanol (7), basically differs from all of the aforementioned sympathomimetics in that the hydroxyl group at C3 of the aromatic ring is replaced with a hydroxymethyl group. It is synthesized in two ways. According to the first(Scheme-1), it is prepared from 4-hydroxy-acetophenone, the chloromethylation of which gives 4-hydroxy-3-hydroxymethylacetophenone (1).

This is acetylated into a diacetyl derivative (2), which is further brominated into the corresponding bromoacetophenone (3). Reacting this with N-benzyl- N-*tert*-butylamine gives a derivative of aminoacetophenone (4), the acetyl group of which is hydrolyzed by hydrochloric acid, and the resulting product (5) undergoes a reduction—first by sodium borohydride for transforming the keto group into a hydroxyl group to give 6, and then by hydrogenation over a palladium catalyst for removing the benzyl-protecting group, giving albuterol (7).

Salbutamol is taken by some as an alternative to clenbuterol for purposes of diet and bodybuilding use fat burning, and/or as a performance enhancer. Abuse of the drug may be confirmed by detection of its presence in plasma or urine, typically exceeding 1000 µg/L.[102-103]



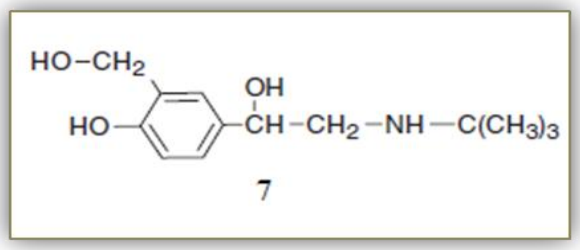


Fig.23: Salbutamolsynthesis

Clinical studies show no compelling evidence that salbutamol and other β_2-agonists can increase performance in healthy athletes.[104] In spite of this, salbutamol required "a declaration of Use in accordance with the International Standard for Therapeutic Use Exemptions" under the 2010 WADA prohibited list. This requirement was relaxed when the 2011 list was published to permit the use of "salbutamol (maximum 1600 micrograms over 24 hours) and salmeterol when taken by inhalation in accordance with the manufacturers' recommended therapeutic regimen".[105-106] According to two small and limited studies, performed on eight and 16 subjects, respectively, salbutamol increases the performance even for a person without asthma.[107-109]

Salbutamol may be quantified in blood or plasma to confirm a diagnosis of poisoning in hospitalizedpatients or to aid in a forensic investigation. Urinary salbutamol concentrations are frequently measured in competitive sports programs, for which a level in excess of 1000 µg/L is considered to represent abuse. The window of detection for urine testing is on the order of just 24 hours, given the relatively short elimination half-life of the drug.[110-111]

Terbutaline

Terbutaline is currently on the World Anti-Doping Agency's list of prohibited drugs for Olympic athletes, except when administered by inhalation and a Therapeutic Use Exemption (TUE) has been obtained in advance.

Terbutaline is currently used to delay preterm labor for 48 hours to allow for fetal lung maturity through steroid injections. It should not be used to prevent preterm labor or delay labor more than 48-72 hours. In February 2011, the Food and Drug Administration has ordered to put a boxed warning on the drug's label. Pregnant women should not be given injections of the drug terbutaline for the prevention of preterm labor or for long-term (beyond 48-72 hours) management of preterm labor, and should not be given oral terbutaline for any type of prevention or treatment of preterm labor "due to of the potential for serious internal heart problems and death."[112-113]

The American College of Obstetricians and Gynecologists also discourages the use of terbutaline for preventing preterm labor.[114]

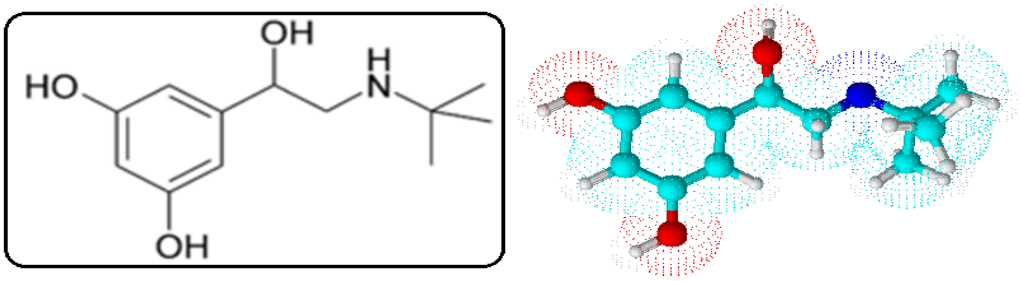


Fig.24: 5-[2-(tert-butylamino)-1-hydroxyethyl]benzene-1,3-diol]

Terbutaline, α-[(*tert*-butylamino)methyl]-3,5-dihydroxybenzylic alcohol (3), differs from the examined compounds mainly in the location of hydroxyl groups in the benzene ring, and is synthesized by brominating 3,5-dibenzyloxyαcetophenone into the appropriate 3,5-dibenzyloxybromoacetophenone (1), which is reacted with N-benzyl-N-*tert*-butylamine, giving the aminoketone (2). Reduction of this product by hydrogen over a palladium catalyst leads to terbutaline (2).

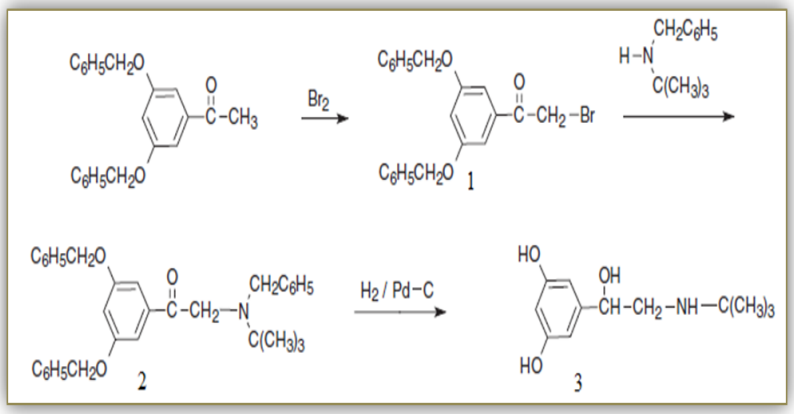


Fig.25: Synthesis of Terbutaline

Terbutaline is a synthetic sympathomimetic amine. It is one of the most selective direct–acting stimulants of β2-adrenoreceptors. It stimulates smooth muscle β2-adrenoreceptors in the bronchi, relaxing them and relatively minutely acting on the β1receptors of the heart. It is used for preventing and relieving bronchospasms in bronchial asthma, chronic bronchitis, pulmonary emphysema, and other broncho-pulmonary diseases. Synonyms, arebretin and bricanyl.

Terbutaline is used as a fast-acting bronchodilator (often used as a short-term asthma treatment) and as a tocolytic[115] to delay premature labor. The inhaled form of terbutaline starts working within 15 minutes and can last up to 6 hours.

Terbutaline as a treatment for premature labor is an off-label use not approved by the FDA. It is a pregnancy category 'B' medication and is routinely prescribed to stop contractions. After successful intravenous tocolysis, little evidence exists that oral terbutaline is effective.[116] However, following uterine inversion in the third stage of pregnancy, Terbutaline (or either Halothane or magnesium sulfate) can be utilized to relax the uterus if necessary prior to uterine replacement.Tocolytic Agents Drugs that prevent preterm labor and immature birth by suppressing uterine contractions (TOCOLYSIS). Agents used to delay premature uterine activity include magnesium sulfate, beta-mimetic, oxytocin antagonists, calcium channel inhibitors, and adrenergic beta-receptor agonists. The use of intravenous alcohol as a tocolytic is now obsolete.[117-118]

8. CONCLUSION

In conclusion, The PED's & Psycho-mimetic agents are all extremely addicting and cause dependency over short and long periods of time.. It is proven that drugs do kill and if not, cause permanent damage to our body and brain. Our brain is affected by drugs immediately and in most cases leaves permanent damage. Long term use may result in changes in brain function that last long after the person stops using drugs. The withdrawal symptoms may last for months or even a year.

After studying above some performance enhancing drugs we can understand that these performance enhancing drugs are mainly invented to cure disease but these are used by the athletes to increase their performance. When these drugs are used by the athletes than after some time they get some side effects from the drugs which cause them some unwanted disease like impotency, cancer and many more. Now a day's some children and adults to gain the muscle and to become smart in looking they use these drugs (like they use creatine to gain muscle) and gain the desired result but due to large use of these performance enhancing drugs they get adverse effects and get spoiled their future. These drugs has been used since ancient time and now a day's also used in the sport but now some Countries banned the use of these drugs in sport if they found anyone using these drugs then they bane him or her in sport and their future in sport is totally spoiled. These drugs are mainly invented to cure disease disorders and to make the patient to feel better like in Asthma salbutamol and terbutaline is used to cure or feel the patient to recover from problem in breathing but these drugs are also used by athlete during large exercise they use these drug to reduce their tiredness in spite of feeling great tiredness due to hard exercise.

So The Performance Enhancing drugs should be used to cure disease only not in sports and not in normal condition to gain muscles or other effects.

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