Sports Pharmacology: A Medical Pharmacologist’s Perspective

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ABSTRACT

Abuse of substances or methods to enhance the performance is becoming very common in the sports, which often destroys the spirit of competition. The regulatory bodies for sports have reported rates ranging from 5% to 31% for the use of performance-enhancing substances among athletes. Athletes can have serious injuries and morbidities, leading to poor health with the use of such substances. Commonly abused agents in sports include anabolic–androgenic steroids and its analogs, blood, erythropoietin, growth hormone and its derivatives, nutritional supplements, creatine, amphetamines, beta-hydroxy-beta-methylbutyrate (HMB), stimulants, and analgesics. Health-care professionals need to be careful while prescribing medicines to sportspersons. Knowledge of exercise physiology, pharmacology of the commonly used agents for sports-related injuries, and agents used for doping could help the sportspersons and health-care professionals to avoid the embarrassment arising because of misuse of these agents. Sports pharmacology includes study of the various aspects of the drug use and abuse in sports and treatment of sports-related injuries. Focusing on sports pharmacology in the medical curriculum can help the upcoming health-care professionals to support the sportspersons to improve the quality of their life by using various drugs and other substances within the standardized limits and avoid embarrassment of doping.

KEYWORDS: Athletes, doping, drug abuse, ergogenic aids, exercise, World Anti-Doping Agency

INTRODUCTION

In the current cutthroat era of sports, where the second winner is viewed as the first loser, the spirit of “fighting well” is lost completely. Winning no longer involves winning the medal and the pride, but the multimillion-dollar deals that come with it in the form of endorsements, appearances, and contracts. Considering this reality, the athletes are ready to sacrifice their integrity and take a risk to gain the competitive edge and enhance the performance.[1] Difference of milliseconds can make one a winner or loser in sports these days. Any advantage to a sportsperson will increase their chance of winning the medal and endorsements in million dollars. In such a cutthroat competition, the use of performance-enhancing substances (PESs) has become increasingly popular. Study of the action of biologically active substances involved with healthy individuals in the form of food or medicines that increase resistance to various adverse factors, and enhance recovery from biological stressors or prevent illness, is called as pharmacosanation.[2] It has been useful in helping athletes deal with the emotional and physical stresses of training and competition.

Sports Illustrated issue of 1997 showed a report, when 198 aspiring US Olympians were asked, if they would take a prohibited PES if they were promised to win and not get caught, 98% said “Yes.” Then, when asked, “Would you take the same undetectable substance if it would contribute to winning every competition for 5 years, then leading to death?”, half of them still said “Yes.”[3] The Bible mentions the first case of use of PES, described in the “Garden of
Eden,” when Adam and Eve ate the banned fruit to gain the divine powers.[4] Painting of the Chinese Emperor Shen-Nung from 2737 BC became the first document related to the use of doping agents, which showed the emperor with leaves of “máuchuang” (Ephedra). Ancient Olympic Games in the third century BC have recorded the use of herbal teas and mushrooms by athletes to increase their performance during competitions. In South America, stimulants such as strychnine and cocaine were used.[5,6]

English cyclist Arthur Linton was alleged to have overdosed on “trimethyl” (compound containing either caffeine or ether) and died in 1886 during a 600-km race. Another English cyclist Tom Simpson died with high blood levels of methamphetamine in 1967. Abuse of albuterol has been rampant with triathletes as it helps them to improve their respiration during competition. Abuse of anabolic steroids is common in sprinters and in sports such as football and baseball. Anabolic steroids make these athletes feel stronger and more powerful. Thus, it was imperative to create the rules banning certain substances from competition.[7]

Well-known athletes were also found to have abused the drugs for enhancing the performance. Usain Bolt, a well-known Jamaican sprinter, is regarded as the fastest human ever timed. He was asked to surrender one of his nine Olympic gold medals as one of his teammate in 4 × 100 m relay, Nesta Carter abused a PES at the Beijing Olympics. All the four members of Jamaica’s 4 × 100 m squad in 2008, namely Bolt, Carter, Asafa Powell, and Michael Frater, lost their medals under the rules of the international association of athletics federations, athletics’ governing body. American track and field sprinter Tyson Gay tested positive for a banned substance in July 2013. This led to his withdrawal from the World Championship in Moscow. He had to serve 1-year ban after testing positive for a prohibited anabolic steroid in 2013, subsequently, he was suspended by the United States Anti-Doping Agency until June 23, 2014. He was also asked to surrender his silver medal from the 2012 Summer Olympics. Maria Luisa Calle Williams was a Colombian professional racing cyclist. Forty-three-year-old Calle won gold medal at the Pan American Games on October 16, 2011. However, on July 22, 2015, it was disclosed that she had tested positive for Heptaminol doping test and was subsequently banned for 4 years.

**Physiological Changes during Exercise**

Vasodilatation of skeletal muscle arterioles and vasoconstriction of the arterioles of inactive areas of the body can occur during exercise. Increase in local temperature, CO₂, lactic acid, and enzymatic activity of the liver leads to increased excretion of drugs with low extraction ratio, for example, caffeine and ibuprofen. Such changes lead to change in pharmacokinetics and pharmacodynamics of certain drugs.[8]

Skeletal muscles are made up of fast-oxidative glycolytic fibers, slow-oxidative fibers, and fast-oxidative glycolytic fibers. Low-intensity endurance events, such as marathon running, make use of slow-oxidative fibers, whereas fast-oxidative glycolytic fibers are used mainly during shorter, higher intensity endurance events, such as in a 1-mile run, as they generate more force but fatigue easily. Fast-oxidative glycolytic fibers are commonly used in highly brisk events, such as the 100-m dash. Rise in the number of mitochondria particularly in the slow-oxidative and fast-oxidative glycolytic fibers and increase in the capillaries around them result because of endurance training. Muscle hypertrophy for fast-oxidative glycolytic fibers is the end result of short-duration, high-intensity exercise, such as weight lifting. Energy for short-duration and high-intensity exercise is derived from the immediate energy system, such as anaerobic glycolysis, adenosine triphosphate, and creatine phosphate, whereas it is mainly provided by oxidative phosphorylation for endurance-type exercise.

Heart rate and stroke volume rise are proportionate with the amount and intensity of exercise. Stroke volume starts leveling off earlier than the heart rate. Increase in stroke volume is the result of increased contractility of the ventricles and increased venous return. The incremental rise in cardiac output goes to the muscles used for exercise, heart, and skin. The capillary density in the muscles and stroke volume increase during endurance training but heart rate tends to decrease with no change in cardiac output at rest. Rise in the systolic blood pressure with either no change or a slight decrease in the diastolic pressure is characteristic in exercise. Decrease in plasma volume owing to increased capillary filtration and increased oxygen consumption by the active muscles are common features observed during exercise. Adequate ventilation and aeration of the blood even in heavy exercise are provided by the respiratory system. Therefore, respiration is mainly controlled by neurogenic mechanisms during exercise. The exercise capacity is usually limited by the ability of the heart to pump blood to the muscles.[9]

Use of medication to alter the physiological changes and enhance the endurance and exercise capacity is not uncommon with sportspersons.

**Doping**

The use of artificial means to improve performance is not exclusive to modern times.[10] The term “doping” was introduced in English in 1889, when a potion containing
opium was abused in horses. Abuse of mushrooms, plants, and mixtures of wine and herb was reported way back in 776 BC by the Roman gladiators and the Greek Olympic athletes competing in Circus Maximus. Various plants and their extracts were abused for enhancing the speed and endurance, masking pain in injured athletes to continue in sports events. Abuse of combinations of stimulants such as caffeine, heroin, strychnine, and cocaine was common among the athletes. Amphetamines replaced strychnine as the preferred stimulant during the 1930s. Later, in the 1950s, male hormones were used by the Soviet Olympic team. International Olympic Committee (IOC) started determined efforts to detect the drug abuse in sports in the 1960s, when a Danish cyclist died during the Rome Olympic Games. East German government’s program of performance enhancement was unearthed by the fall of Berlin Wall. A wide range of banned substances, including erythropoietin, was found in 1998 by the police in a raid at the Tour de France.

In 1999, the World Anti-Doping Agency (WADA) was established to monitor, coordinate, and promote the fight against doping in all forms of sports. It consists of experts from various disciplines including sports medicine, pharmacologists, physiologists, pharmacists, geneticists, and laboratory scientists. A list of banned substances by the IOC is given in Table 1. The WADA releases an updated list of banned substances every year, which is available on their website (www.wada-ama.org). The WADA classifies doping as substances and methods prohibited at all times (in-competition and out-of-competition [OOC]), substances prohibited in competition, and substances prohibited in a particular sport. The categories of the drugs included in subsequent classes are given in Table 2.

In sports, as mentioned by the WADA, the term “doping” refers to any of the following cases:

- Presence of a banned substance or its markers or metabolites in the athlete’s sample
- Use or attempted use of banned substances or methods by an athlete
- Failure or refusal or evading to submit sample collection
- Failure to file missed tests and whereabouts
- Interference or attempting to interfere with any part of doping control
- Trafficking or attempted trafficking of any prohibited substance or method
- Administering or assisting a prohibited substance to a sportsperson
- Encouraging, supporting, abetting, covering up, or any other type of intentional complicity

The use of drugs by any sportsperson to enhance his/her performance is considered unethical, and hence prohibited by most of the international sports organizations, including IOC. Apart from causing serious health issues and permanent neurological disorders to the sportsperson, it is also against the sporting spirit and destroys the integrity of sport itself.

Exemption to the use of prohibited substance or method is allowed, if an athlete with documented medical conditions requires the use of a prohibited substance or a prohibited method under a therapeutic use exemption (TUE) requisition. The therapeutic Use Exemption Committee reviews all the applications for a TUE under the specified criteria for granting TUE.

### Table 1: Examples of banned substances by the International Olympic Committee

| Category                  | Examples                                                                 |
|---------------------------|-------------------------------------------------------------------------|
| Stimulants                | Amiphenazole, amphetamine, amphetamines, bupropion, bromantan, cocaine, caffeine, ephedrine, fencamfamine, methylphenidate, mesocarb, pipradrol, pentetrazol, salbutamol, strychnine, terbutaline |
| Narcotics                 | Buprenorphine, dextromoramide, diamorphine (heroin), meperidine, methadone, morphine, pentazocine |
| Beta blockers             | Acebutolol, alpredolol, atenolol, betaxolol, esmolol, labetalol, metoprolol, nadolol, oxprenolol, sotalol |
| Masking agents            | Bromantan, epistosterone, probenecid                                    |
| Diuretics                 | Acetazolamide, bendroflumethiazide, bumetanide, chlorothalidone, canrenone, ethacrylic acid, furosemide, hydrochlorothiazide, spironolactone, triamterene |
| Peptide hormones, mimetics, and analogs | Corticotrophins, erythropoietin, human chorionic gonadotropin (prohibited only in male athletes), human growth hormone, insulin (permitted only with certified insulin-dependent diabetes), insulin-like growth factor (IGF-I), pituitary and synthetic gonadotropins (e.g., luteinizing hormone—prohibited only in male athletes), clomiphene (prohibited only in male athletes), cyclofenil (prohibited only in male athletes), tamoxifen (prohibited only in male athletes) |
| Anabolic steroids/beta 2-agonist/anabolic agents | Androstenediol, androstenedione, bolasterone, boldenone (dihydrotestosterone), clenbuterol, clodexol, danazol, dehydrochloromethyl-testosterone, dehydroepiandrosterone, dihydrotestosterone, drostanolone, ethylestrenol, formebolone, fluoxymesterone, furazabol, mesterolone, metandienone, methandriol, methyl-testosterone, nandrolone, oxandrolone, 19-norandrostenediol, 19-norandrostenedione, norethandrolone, oxandrolone, oxymesterone, oxymetholone, stanozolol, stenbolone, testosterone, trenbolone |
A sports performance is based on four dimensions: skill, strength, endurance, and recovery. Different sports require a different blend of these four dimensions for a high performance. Different PESs/performance-enhancing drugs (PEDs) offer benefits along these dimensions.[12] An overview of the commonly used PESs is given below.

### Anabolic and androgenic agents

Anabolic–androgenic steroids as the name suggests, have anabolic effects, which lead to its abuse for the enhancement of sport performance.[7,13,14]

Gonadal steroids (i.e., androgens and estrogens) play an important role in bone metabolism throughout life in both men and women. Their actions include growth, development, and maintenance of reproductive organs, promotion of protein synthesis leading to increased muscle mass and weight, masculinization, general growth, and bone maturation.[15]

Nandrolone is an injectable anabolic–androgenic steroid with long half-life, which allows the detection of its metabolite products. Testosterone administration is commonly analyzed by means of the ratio between epitestosterone glucuronide and testosterone glucuronide, known as “T/E ratio.” Dihydrotestosterone is an endogenous substance that can be used to promote anabolic effects because of its high affinity to the androgenic receptor. Indirect androgen doping can be carried out by using agents such as clomiphene, raloxifene, and toremifene, or aromatase inhibitors such as aminogluthethimide, anastrozole, letrozole, and exemestane. Steroid precursors, particularly anabolic steroid precursors or prohormones, have gained popularity as PEDs in the past 15 years.[7,13-15]

### Glucocorticoids

Glucocorticoids are natural and synthetic hormones, steroid in nature with anti-inflammatory properties. They are responsible for anabolic actions, which include stimulation of gluconeogenesis and utilization of amino acids and fatty acids, reduce tiredness, relieve fatigue and inflammation, act as mental stimulant, and increase tolerance for pain. Glucocorticoids mediate ergogenic effects in humans and animals, thus, they remain on the WADA’s list of banned products. TUE can be considered if declaration of use by the athlete is provided. Topical preparations of glucocorticoids, when used for nasal, ophthalmic, auricular, buccal, dermatological (including iontophoresis/phonophoresis), gingival, and perianal disorders are not prohibited and do not require TUE or a declaration of use.[7,13-15]

### Beta agonists

Beta agonists are phenylethanolamines with different substituent on the terminal amino group and the aromatic ring. They are banned for their stimulant and anabolic effects, and their use by athletes is restricted until a valid medical permission is obtained in advance.[14] Salbutamol, a beta-adrenergic agonist is permitted by inhalation for the asthma treatment. Inhaled salbutamol is not easy to evaluate by urinalysis if unauthorized systemic administration has been used.[16]

### Beta blockers

The actions of beta blockers include reduction in heart rate and muscle tremors, which may improve performance in specific sports requiring steadiness and accuracy, such as archery and shooting. These agents have deleterious effect in endurance sports.[17]

### Stimulants

Stimulants have direct and peripheral effect on the nervous system. Substances that temporarily excite or accelerate physiological activity are called stimulants. These agents increase alertness, reduce fatigue, and affect mood and cardiovascular activation.[14,15] Caffeine is known to counter drowsiness, improve endurance, and enhance bodybuilding exercise. Recently published meta-analysis by Grgic et al, showed significant
Ergogenic effects of caffeine ingestion on maximal muscle strength of upper body and muscle power.[18] Methylphenidate is extensively transformed into ritalinic acids, which because of its chemical properties escape traditional detection of stimulant drugs.[19]

**Peptide hormones, growth factors, and related substance**

Hormones get metabolized rapidly and hence have a very short half-life. They are excreted in less quantity as unchanged compounds in the urine. Growth hormone (GH) or somatotropin is a polypeptide hormone secreted by the anterior part of the pituitary gland.[14,20]

The actions of GH include increase in lean body mass, energy, performance, muscle mass and strength, stroke volume, and maximal oxygen uptake. Its abuse in sports is increasing as it is difficult to detect.[21]

Analyzing the insulin concentration in blood is important in doping control in athletes as the administration of exogenous insulin enhances the athlete’s performance. Bodybuilders, weight lifters, and powerlifters use short-acting insulin to increase muscle bulk. IOC banned its use except TUE.[22]

Erythropoietin is a peptide hormone known to act on bone marrow and stimulate red blood cell production. It can increase VO\textsubscript{2max} by 20%.[23] Recombinant human erythropoietin (epoetin alfa and darbepoetin) can also be used to increase the oxygen-carrying capacity of blood and to boost the performance in sports such as running, cycling, and skiing where endurance is the key for performance.[23]

Human chorionic gonadotropin is a glycoprotein hormone secreted by placenta and responsible for the development of sexual glands. It is used to raise gonadal testosterone synthesis during and after self-administration of testosterone or anabolic steroids. Its use is prohibited only in male athletes.[14,15,24]

**Blood doping**

Blood doping means the abuse of certain methods or substances or both to increase the oxygen delivery to muscles and the aerobic capacity of athletes to get the competitive edge in sports activities. It may include autologous or homologous blood transfusions, administration of erythropoiesis-stimulating agents such as erythropoietin, or blood substitutes such as perfluorocarbons and hemoglobin-based oxygen carriers.[25]

It is easily available, difficult to detect, and hence used commonly by athletes. Particularly, autologous blood transfusion is difficult to detect. Indirect detecting methods such as measuring total hemoglobin mass (red blood cell size) or metabolites of blood bag plasticizers (by-products of the container the blood is stored in) can be used in such cases.[26]

**Gene doping**

The nontherapeutic use of genes, cells, genetic elements, or change of gene expression, having the capacity to improve performance in sports is called gene doping. Mostly, it is an intentional use of gene therapy to enhance an athlete’s performances.[27] The genes are added or modified not to prevent or treat illness but only to influence the performance.

**Amphetamine derivatives**

Several different compounds are converted into amphetamines in the human body. Finding amphetamine in urine may indicate ingestion of either amphetamine itself or one of those compounds. Drugs such as cocaine, amphetamines, and hallucinogens can modify mental alertness. By central actions, these agents can increase alertness, or impart motivational and attitude advantage.

By peripheral actions, it can increase cardiac output, blood flow to muscles, and thus influence the performance at least in the early stage of exercise.[28] In the urine, no unchanged cocaine is normally found. The main metabolic products found are benzoylecgonine and ecgonine methyl ester.

**Narcotic analgesics**

Narcotic analgesics are often used for pain control as they interact with specific receptors and manage the neural axis for pain. They mainly depress the nervous system to reduce fear, anxiety, and pain sensations, which allow the athletes to perform beyond their normal pain threshold. High pressures on the athletes to perform competitively, leading to several musculoskeletal injuries are the outcome of abuse of these substances. Buprenorphine, with its low-therapeutic dose and relatively long-elimination period, has low concentration in urine and is usually detectable only by immunoanalytical methods. Hence, it is not easy to confirm by mass spectrometry.[29]

Codeine is permitted as an antitussive drug. Nevertheless, 24 h after administration, it is converted partially to morphine, which is a forbidden drug.[13-15,29]

Dextromethorphan is an antitussive drug, which is converted metabolically into dextorphinan, the D-isomer of \textit{\textsuperscript{\textalpha}}-levorphanol, a forbidden narcotic drug. Distinguishing between a licit and an illicit use may be problematic.[13-15]

**Diuretics**

Diuretics are often used to lose weight quickly to compete in lower weight category or as a “masking agent,” that is, to reduce the concentration of other banned substances in urine as it enhances the speed of elimination of PEDs. Anabolic steroids can cause fluid retention, which the diuretics can overcome, and hence commonly abused along with steroids. However, deleterious effects such as electrolyte imbalances, muscle cramps, dehydration,
and volume depletion, leading to death are serious consequences of diuretic use. Detection techniques for diuretics are highly sensitive.\textsuperscript{[13-15,17]}

**HMB**

Beta-hydroxy-beta-methylbutyrate is a by-product of metabolism of amino acid leucine. It is also a progenitor to cholesterol. It impairs protein metabolism after workouts and has recently gained greater attention among the athletes.\textsuperscript{[13-15]}

**Alcohol**

In-competition use of alcohol is prohibited. The doping violation threshold (hematological values) is 0.10 g/L for alcohol. It decreases nervousness, anxiety, and hand tremors, which are particularly useful in the sports such as archery and shooting. However, it adversely affects reaction time, leading to unsteadiness of the limbs and sedation effects, which makes it particularly threatening in sports such as vehicle racing.\textsuperscript{[16]} Alcohol has been removed from the prohibited list in 2018, it was previously banned in four sports. National Anti-Doping Organizations will no longer be obliged to conduct tests for alcohol but are able to assist governing bodies when considered appropriate.

**Important changes in WADA 2018 list of prohibited substances**

Alcohol has been removed from the prohibited list. Cannabidiol has also been removed from the prohibited list, unless it contains THC (Tetrahydrocannabinol). A synthetic actoprotector, Bemitil has been added to the WADA monitoring list in and out-of-competition, while hydrocodone will be monitored in-competition. Mitragynine and telmisartan are removed from the monitoring list.

**Laboratory Testing**

Sample collection for testing is carried out in one of the two ways, “in-competition” testing (at an event) and “out-of-competition” (OOC) testing (at squad sessions, home, or training venue). No specific method of selection of athletes for testing is considered, rather their positions are randomly selected. Automated draw is used to select the athletes for OOC selections. The testing needs to be carried out at WADA-accredited laboratories. During the test, the athletes provide their identification and two samples under direct supervision. Sample A is analyzed for banned drug or methods, whereas sample B is used only if sample A is positive and the athlete wants analysis to be confirmed.

Evolution of the concept of personalized biomarker monitoring has led to “Athlete Biological Passport.” It is designed to detect the changes in hematological, steroidal, and endocrine profile of the athlete. Any deviation of a biomarker from the normal range can be attributable to doping or a medical condition. As health-care professionals use disease-related biomarkers to diagnose the pathology, specifically selected biomarkers can be used to detect doping.\textsuperscript{[33]}

**Getting Away with Doping**

With hundreds of drugs appearing on the “prohibited list” of WADA, it becomes a daunting task to collect the biological specimens from athletes and analyze them for PEDs. Bio-specimens such as urine or blood samples have to be obtained from the athletes. This involves multiple samples being collected and processed, some for immediate analysis and others stored for later confirmatory analysis (if required). These bio-specimens then have to undergo complex and precise biochemical analysis procedures to test for the banned PEDs. In addition, it is not practically possible to collect samples from all the athletes participating in sport events across the world.

Sportspersons try various methods to avoid being caught for doping. Some athletes use a device to give false sample of urine for tests. The device contains a balloon with maneuvered clean urine. The balloon is put in the anus of the athlete before the competition starts. The catheter remains imperceptible below the perineum. During the collection of urine sample in doping control room, the athlete can contract the gluteus and elevator muscle of anus, eliminating the fake urine sample. This fake urine sample can give rise to false-negative results. Use of masking agent is another way to escape. These masking agents can speed up the elimination of PEDs or even mask the detection of the PEDs in the sample to be analyzed. Another strategy used by the athletes to avoid detection is to wait for adequate “washout” period. In this case, the athletes use PEDs during their training period to enhance the amount of intensive exercise that they can perform. This enhanced training leads to improvements in their endurance and muscular strength. The athletes can stop taking the PEDs, keep on training, and wait for metabolic clearance of the PEDs. The athletes lose some benefit because they have stopped taking the PEDs, but they have still improved their overall physical fitness level because of their enhanced training while on the PEDs. This fitness improvement will diminish over time, but enough residues may remain, which may give a slight advantage during a competition to the associated athlete.

Finally, some athletes are inventive and are constantly seeking out new drugs or procedures to gain an advantage. They look for PEDs that are not on the
WADA prohibited list, and hence will not be tested for in the collected bio-specimens. Later, WADA might add such new PEDs to its listing, once a scientific investigation shows that they should be banned, but until then, its use and detection might not lead to an athlete’s disqualification. It is important to remember that pharmaceutical companies have a multitude of drugs in the research and development, although they might be developed for valid medical reasons, these drugs can have direct or indirect biochemical and/or biological actions (i.e., side effects), which can cause the athletes’ physiology to alter in such a way that their sports performance is improved. In other words, sometimes athletes are staying one step ahead of the scientists in trying to find and seek out new PEDs.[32,33]

**Sports-Related Injuries**

Most sports injuries are due to either overuse of muscles or joints or physical injury. Most of the injuries are caused by a slight trauma to the bones, muscles, joints, ligaments, or tendons, including contusions or bruises, sprains, and strains. Ankle joint is the most common site for strain or sprain. The most common sports-related injuries include tennis elbow (lateral epicondylitis), golfer’s or baseball elbow (medial epicondylitis), lumbar strain (trauma to the lower back resulting in injured tendons and muscles that cause spasm), jumper’s knee (patellar tendonitis), runner’s knee (patella–femoral stress syndrome), fractures, stress fractures, and dislocation. Tennis elbow received international recognition when the famous Indian cricketer Sachin Tendulkar had it.[34]

**Rehabilitation for Sports Injuries**

Type and seriousness of injury decides the entire recovery program for sports injuries on the basis of sportspersons’ individual needs. Integrated approach with active involvement of injured athlete and family is very important for the success of recovery program. In case of amputation, achieving highest level of function and gaining independent movements are the primary goals. Improvement in the overall quality of life is also an important objective. The recovery programs, which help to achieve these goals, have components such as exercise programs to stretch and strengthen the affected area, restrictions of movements, physical or occupational therapy, and conditioning exercises to help prevent further injury. It can also include hot or cold applications to the affected area, Jacuzzi treatments, and application of braces, splints, or casts to immobilize the area, and if required, use of crutches or wheelchairs. Pain management techniques and patient and family education also form an integral part of the rehabilitation program.[35]

The medication for pain management needs to be administered cautiously in the athletes. Drugs such as nonsteroidal anti-inflammatory drugs (NSAIDs) can be controversial as it can reduce inflammation but may impair muscle-healing process, resulting in decreased muscle pliability and force production. However, NSAIDs do not have any adverse effect on ligament healing, and may even increase the early ligament strength when given for the first 6 days. NSAIDs shown to have delayed the fracture healing in some animal studies, have no evidence in the humans.[36] Fracture healing involves differentiation of mesenchymal cells to osteoblasts and chondrocytes progenitors.[37] Cyclooxygenase pathway, which is responsible for the synthesis of various prostaglandins, plays an important role in osteogenesis and chondrogenesis. Inflammation modulators can be used as an alternative to NSAIDs as they regulate and control the inflammatory process by inhibiting pro-inflammatory cytokines and stimulating anti-inflammatory cytokines. Traumeel is the first marketed inflammation modulator which contains fixed combination of biological and mineral extracts. Topical glyceryl trinitrate, aprotinin injections, botulinum toxin, and prolotherapy can be used as an alternative to NSAIDs in the treatment of soft tissue injuries.[38] Injection of a sclerosant such as hypertonic glucose or phenol at the injury site is called as prolotherapy. Aprotinin is a small protein bovine pancreatic trypsin inhibitor (BPTI), or basic trypsin inhibitor of bovine pancreas, which acts as antifibrinolytic molecule that inhibits trypsin and related proteolytic enzymes. It is used in treatment of soft tissue injuries. Metalloprotease inhibitors are cellular inhibitors of the matrix metalloproteinases (MMPs). They are also gaining importance in treatment of soft-tissue injuries.[38]

To take care of such situations, pharmacy services were created at the London 2012 Olympic and the Paralympic Games. They were among the most advanced and comprehensive of any Olympic and Paralympic Games.[39]

**Sports Pharmacology and Sports Pharmacy**

Sports pharmacology involves the study of medicine pertaining to sportspersons and plays a vital role in athletics. It includes regular health assessment and management of medical history of the people involved in sporting activities and the treatment of sports-related injuries.[40] Athletes and sportspersons can prevent...
illness, injuries, and incidences of doping through the basic knowledge of sports science, exercise physiology, and pharmacokinetics and pharmacodynamics of biologically active substances that enter their body in the form of food or medicines.\[^{[41]}\]

The medical education in India is generalist in nature, and therefore produces graduates who have knowledge and skills across the whole range of preclinical, paraclinical, and clinical medicine. It is at the postgraduate level that they become specialists in disciplines such as medicine, surgery, pediatrics, or pharmacology. Even the postgraduate courses in pharmacology do not provide enough exposure to sports pharmacology. With the increasing involvement of medicine in sports, it is clear that a specialized training in the field of sports medicine for pharmacologists is required.

In addition, the pharmacists can use their expertise in drug selection and dosing to meet the unique needs of athletes for treatment and preventative care. Training them on these aspects constitutes sports pharmacy.\[^{[42]}\] Such sports pharmacists can be a good resource to the athletes for information on dietary supplements and prescriptions. Sports pharmacologists and pharmacists together can form a community to support doping-free sports in India.

**Role and Importance of Sports Pharmacology**

Both drugs and exercises produce different kinds of physiological actions in the body, which may or may not affect the performance and wellness of the athletes. For example, over-the-counter medications for common cold taken by athletes contain chemicals that can accelerate the heart rate, nervousness, and cause other reactions. Such side effects particularly when the athletes are exercising can reduce their ability to perform and put them at risk. Nutritional supplements used by the athletes can also lead to inadvertent doping.\[^{[43-45]}\]

Hence, it is extremely important for the athletes to be very cautious about their intake. Extent of drug effect depends on various factors such as route, dosing frequency, duration, and dosage form of drug. The way in which a drug enters the organ or tissue too, greatly influences its effect. Medications from alternative therapies such as Ayurveda can also have an impact on the athlete's performance.\[^{[46-47]}\] Use of herbal medicines and nutritional supplements has been on the rise particularly in India. These substances contain various polyphenols, terpenoids, and alkaloids which can have beneficial physiological changes in athletes e.g. Ginseng as an endurance performance enhancer.\[^{[48]}\] Currently, there are no recommendations or guidelines on use of such substances in sports. Hence it is very much necessary to know pharmacology of different drugs.\[^{[49]}\]

Health-care professionals now have to be more careful while prescribing drugs to the sportspersons because some of the drugs are banned by the IOC, National Collegiate Athletic Association, and other athletic organizations. If athletes approach health-care professionals as ordinary patients then there is a high possibility of missing out the potential doping issue with the prescription of drugs.\[^{[49]}\] Athletes who test positive for the prohibited drugs can be disqualified from the sporting event, suspended for a defined period, or may get lifetime ban. No to drug abuse is the safest possible alternative for athletes to have a fair competition and success. The necessity of athletes to know the drug, its exact effect, and the prescribed limit, led to the introduction of pharmacology in sports. Sports pharmacology also forms an integral part of forensic pharmacology.\[^{[50-52]}\] As the sporting spirit is gaining momentum across the globe in the recent years, the awareness of fair play in sports is also increasing. Sports pharmacology is playing a very important role in helping the sportspersons to achieve definite outcomes, which will improve the quality of their life by using various drugs and other substances (well within the standardized limits), enhance their performance, or alter their mood. Though global data are available on doping, Indian data are very limited, and there is a scope to expand research in this domain. Beotra\[^{[53]}\] discussed the doping in sports way back in 1995 in the *Indian Journal of Pharmacology*.

Sports medicine is a broader discipline and contains exercise physiology, surgical and medical management of sports-related injuries, and the use of PEDs.\[^{[54]}\] The very few institutes in India offering courses on sports sciences are mentioned in Table 3. These courses need to be structured, accredited, and regulated by the recognized bodies such as the Medical Council of India or the National Medical Commission. Inclusion of “sports pharmacology” in the medical curriculum will certainly help the upcoming health-care professionals to have a better understanding of the precautions, while using the medications in sportspersons. Medical pharmacologists with their expertise can play an important role if also trained on “sports pharmacology.” Globally, this subject is well recognized, and dedicated courses are available with many well-known universities, some of them are mentioned in Table 4.

Interprofessional learning is essential among the health-care professionals to safeguard the sportspersons...
from inadvertent doping. Sport pharmacologists and sport pharmacists can work in collaboration with other health-care professionals to help this cause by communicating the hazards of inadvertent drug abuse in athletes on regular basis. In addition, such practice of interprofessional collaboration can help in improving the health outcomes. Training on basic principles of teamwork in sports can help health-care professionals regarding possible improvement in strategies and barriers in the optimization of professional collaboration.[55]

Thus, to conclude, health-care professionals with the knowledge of sports pharmacology act as a facilitator between the doping control agencies and athletes. It benefits the athletes not just by improving their overall health and performance, but also by lowering their chances at getting marked into any kind of doping activities, and accordingly maintains the spirit and integrity of the game. Indian authorities need to consider including this subject in medical curriculum for undergraduates or postgraduates.

Table 3: Institutes/universities offering training or research on sports medicine in India

| Institutes/universities | Courses (duration)                     |
|-------------------------|----------------------------------------|
| 1. Indian Association of Sports Medicine (IASM), Faculty of Sports Medicine & Physiotherapy, Guru Nanak Dev University, Amritsar | 1. Doctor of Medicine in Sports Medicine (3 years) |
| 2. Armed Forces Medical College, Pune | 2. Postgraduate Diploma for Medical Graduates (2 years) |
| 3. Netaji Subhas National Institute of Sports, Patiala | 3. Fellowship in Sports Sciences (6 months) |
| 4. Sri Ramachandra Medical College and Research Institute (Deemed University), Chennai | 4. MSc Sports Medicine (2 years) |
| 5. Medvarsity Online, Hyderabad | 5. Fellowship in Sports Rehabilitation (185 hours) |
| 6. Alagappa University, Karaikudi and University of Madras, Chennai | |
| 7. Hospital for Orthopedics, Sports Medicine, Arthritis, and Accident-Trauma (HOSMAT), Bangalore | |
| 8. All India Institute of Hygiene and Public Health, Kolkata, University of Calcutta, Kolkata | |
| 9. University of Pune, Pune | |
| 10. SNDT Women’s University, Mumbai | |
| 11. Vidya Sagar Technological Institute of Physical Education & Sports, Nazir Bazar, Purba Medinipur, West Bengal | |
| 12. Vardhaman Mahavir Medical College, New Delhi | |
| 13. Indian Institute of Sports Medicine (IISM), Dr. MGR university, Chennai | |
| 14. Aryabhatta Knowledge University (AKU), Patna | |

Table 4: Institutes/universities offering training/research on sports medicine outside India

| Institutes/universities | Courses |
|-------------------------|---------|
| 1. International Federation of Sports Medicine, Lausanne, Switzerland | 1. Postgraduate Courses on Sports Medicine |
| 2. Asian Federation of Sports Medicine, China | 2. Team Physician Advanced Course |
| 3. RMIT University, Australia | 3. Team Physician Development Course |
| 4. University of Central Lancashire, UK | 4. Sports Rehabilitation Course |
| 5. University of Western Australia, Australia | 5. Doping Control Officers Course |
| 6. University of Queensland, Australia | 6. Sports and Exercise Cardiology Course |
| 7. Ball State University, USA | 7. Drugs in Sport—Online course |
| 8. University of Otago, New Zealand | 8. Fellowship in Sports Sciences |
| 9. Queen Mary University of London, UK | 9. Master of Science in Sports and Exercise Medicine |
| 10. Middlesex University, UK | 10. Postgraduate Diploma in Sports and Exercise Medicine |
| 11. Murdoch University, Australia | |
| 12. University of Auckland, Australia | |
| 13. University College of London, UK | |
| 14. Liverpool John Moores University, UK | |
| 15. University of South Wales, UK | |
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