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Review Article

Novel technologies in detection, treatment and prevention of substance use disorders

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ABSTRACT

Substance use disorders are a widely recognized problem, which affects various levels of communities and influenced the world socioeconomically. Its source is deeply embedded in the global population. In order to fight against such an adversary, governments have spared no efforts in implementing substance abuse treatment centers and funding research to develop treatments and prevention procedures. In this review, we will discuss the use of immunological-based treatments and detection kit technologies. We will be detailing the steps followed to produce performant antibodies (antigens, carriers, and adjuvants) focusing on cocaine and methamphetamine as examples. Furthermore, part of this review is dedicated to substance use detection. Owing to novel technologies such as bio-functional polymeric surfaces and biosensors manufacturing, detection has become a more convenient method with the fast and on-site developed devices. Commercially available devices are able to test substance use disorders in urine, saliva, hair, and sweat. This improvement has had a tremendous impact on the prevention of driving under influence and other illicit behaviors. Lastly, substance abuse became a major issue involving the cooperation of experts on all levels to devise better treatment programs and prevent abuse-based accidents, injury and death.

1. Introduction

Substance use disorders represent a worldwide problem that is growing substantially over time. It is a social, economic and medical plague threatening the population with an increasing percentage of people becoming addicted. Addiction is normally met by treating the mind through psychological approaches, but in some cases, a combination with pharmacotherapy is necessary [1]. However, these methods

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are not effective and present a great challenge to develop a successful therapy. Therefore, a great deal of interest is given to research and development of innovative approaches. Lately, immunotherapy showed a promising prospect in the treatment of substance use disorders.

The majority of drugs that are abused (such as nicotine, morphine, cocaine, and methamphetamine) depend on their passage to the brain and the feeling of a reward given to the substance user. Therefore, immunotherapy, which is based on the general concept of immunology, aims to produce vaccines by confronting the body with foreign substances. The antigens are identified; then, specific antibodies will be produced against them. After binding with the substances, antibodies will hinder the passage of the antigens through the encephalic barrier and henceforth reduce their psychoactivity [2]. The aim is that immunotherapy would be able to sever the relation between the intake (substance) and the rewarding effect (feeling high), thus facilitating the acceptance of the psychotherapeutic treatment and breaking the addiction habit [2].

Drug molecules are known to possess a small molecular weight; therefore, they do not possess any immunogenic characteristics, which allow researchers to attach carrier proteins of an estimated size to stimulate the immune system. Some early conjugates have been undertaken with albumin, Keyhole Limpet Hemocyanin (KLH) and also tetanus toxoid (TT). The resultant conjugates of the substance-carrier protein are of a size that prevents passage through the brain barrier and therefore preventing the effects expected from the substances of abuse [3–5].

Immunotherapy can be either passive or active. Since passive immunotherapy uses previously prepared monoclonal antibodies and is more useful in cases of overdosing, active immunotherapy is based on immunization, inducing an immunologic reaction to the substance and producing specific antibodies through B-cell memory. However, this type of treatment takes longer to attain the desired results [3,4,6].

Drug use detection has seen a great evolution over the past few decades. It is generally conducted through analysis of a drug or one of its metabolites depending on the analyzed medium. It is a critical process because some metabolites might be present in urine for longer durations compared to blood. The most performant drug detection methods are, in part, based on immunological principles. This had contributed greatly to the elaboration of on-site detection kits with the aim of preventing accidents due to substance abuse.

Currently, researchers are developing many vaccines and/or antibodies that can act on opioids, nicotine, cocaine, heroin, and methamphetamine. In addition, extensive work is being undertaken on new detection technologies. Positive results observed in preclinical studies have led to clinical trials consisting of various stages (concerning cocaine, methamphetamine and some others) [7]. In this review, we will address the importance of immunotherapy approaches and the steps taken in the development of a vaccine with the emphasis on the examples of cocaine and methamphetamine. In addition, current detection technologies, as well as technology-based prevention methods regarding substance abuse and their eventual impact, will be discussed.

2. Immunotherapy for substance abuse detection and treatment

2.1. *Behind the vaccines*

Generally speaking, drug vaccine effectiveness is linked to the quality and quantity of the produced antibodies. In ideal conditions, an effective vaccine elicits a rapid induction and production of large quantities of antibodies to counter the drug circulating in the bloodstream. This will prevent the drug from passing to the brain where most of the pharmacological effects will occur (Fig. 1). It is an attractive concept to simply block the drug molecules in the system, however, when addressing substance use disorders, attention should be paid to other factors. For example, multiple molecules may be used in different doses with distinctive administration routes. Cocaine and nicotine are considered as a perfect example to illustrate the former statement. Cocaine is generally used sporadically, while nicotine is usually consumed regularly in higher doses through the use of tobacco products. Nevertheless, the use of simple blockage against abuse molecules by antibodies in a dose-dependent manner should be considered useful. However, a high antibody dose administration might induce a masking of drugs because of the greater density and saturation [8].

Substances of abuse, such as cocaine and methamphetamine, are of a small size and do not possess antigenic properties to induce an antibody response; therefore, it is necessary for them to be biochemically modified by attaching (conjugating) an immunogenic protein or a carrier to be able to induce an immune response.

To maintain access to drug molecule epitopes in the immunization process, the conjugation of the carrier is carried out with a linker sequence. The latter is linked to the substance from different sites depending on the native structure, and the carrier-linker-substance is chemically attached to form a hapten. This formulation is purified to eliminate the excess free molecules, linkers and –carriers, and then mixed with an adjuvant, such as Alhydrogel, alum or Freund's complete/incomplete adjuvant. The administration of vaccine is generally carried out intraperitoneally or intramuscularly. It is also envisaged that a devised boosting administration program is applied to attain a suitable level of antibodies. This is due to the inefficiency of a single administration of the vaccine to sufficiently stimulate the immune system. Furthermore, in research, various combinations between different types of carrier proteins, linker structures, and adjuvants have been prepared and tested on animals; then, the optimal combination is subsequently selected for testing on humans. Ideally, a proposed vaccine should present no side effects or as minimal as possible. The antibodies produced must be of a high affinity and sufficiently able to react specifically with pharmacologically active doses of native drug forms. This is of utmost importance for the antibodies to ignore the inactive drug metabolites that might compete for the antibodies and thus decrease the binding efficacy. It is also extremely desirable to possess a minimal binding capacity to linkers because these antibodies are likely to bind free drugs in the blood [7].

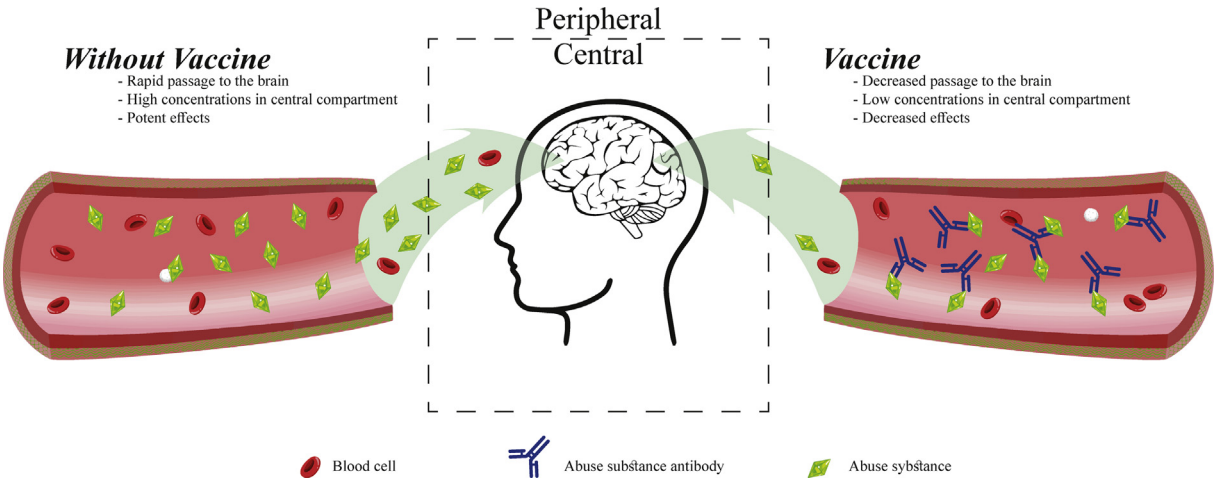

Fig. 1 – The therapeutic approach to vaccines. Mechanism of action of substance abuse in the presence or absence of vaccines.

Research studies have demonstrated the importance of hapten and linker design, conjugation process, carrier choice, and adjuvant use in the development of improved anti-illicit substance anti-bodies and vaccine efficacy. Consequently, work continues with the aim of ameliorating the final product by testing numerous combination and protocols [9–12]. Thus, in order to produce the optimal vaccine, the aforementioned criteria should be well understood and considered.

2.1.1. *Improving antigens creation processes*

Hapten design is the key component in generating highly specific antibodies. It is an overly complex process including the selection and screening of a series of haptens containing different structural modifications. They can attach to linkers from different positions and the biochemical linking process is equally important when coupling to proteins. A relation between hapten stability and high post-immunization anti-cocaine antibody production and their vaccine efficiency has been shown previously [13].

The use of hapten enantiomers has been shown to improve the quality and quantity of the antibody production after immunization, thus suggesting a favorable inclination of researchers to use enantiomers in vaccines, rather than racemic mixtures [14]. Nevertheless, other hapten modifications, such as fluorination [13] or clustering [15] have been explored with the hope of developing more potentially effective strategies of vaccination. This information suggests that the massive efforts spent on hapten development will be able to generate haptens that are structurally and chemically more effective. To summarize, the chemical structure of haptens, linker types and their attachment positions, conjugation reaction, and the purity of the produced hapten are of immense importance in the immunogenic behavior and efficacy of vaccines for drugs.

2.1.2. *Carriers in substance abuse immunotherapy*

Drug vaccine preparation has used a broad range of carrier proteins such as tetanus toxin (TT), keyhole limpet hemocyanin (KLH), Cholera Toxin B (TBC), recombinant exotoxin A from *Pseudomonas aeruginosa* (rEPA), virus-like particles (VLP) or even some peptide-based carriers [12,16–19].

In some opioids vaccine developments, different carriers were tested to screen the best type of antibody producer. The carriers used included bovine serum albumin (BSA), KLH, TT and modified TT, and peptides [20–22]. For instance, research on methamphetamine vaccine development using either KLH or TT showed a tremendous potential in blocking the passage of the abuse substance to the brain. It decreased many of the effects induced by methamphetamine administration including cravings [17,23–26].

In some cases, carriers might possess adjuvant-like characteristics; for example, the cross-reactive material 197 diphtheria toxin (CRM_{197}) [27]. In the case of the cocaine vaccine, a comparison between KLH use and TLR5 agonist flagellin showed higher antibody level with more specificity for the latter conjugate [28]. Another approach is combining with adenoviruses, a disruption of adenovirus is performed by chemical treatment and heat, and then the resultant is conjugated to haptens. Cocaine vaccine prepared from recombinant E1- E2-replication-deficient serotype 5 adenovirus (Ad5) showed promising results and is the subject of a clinical study [29].

The development and use of efficient immunogenic carriers with appropriate characterization and adjuvant-like effects will ultimately produce highly-performant vaccines. This structural management will be useful in hapten/carrier ratios that can be utilized in large-scale industrial production [30].

2.1.3. *Adjuvants*

Freund's complete and incomplete adjuvants are the most widely used adjuvants for vaccines. In addition, aluminum species, monophosphoryl lipid A (MPLA), and class B CpG oligodeoxynucleotides (a TLR9 agonist) are being used in recent vaccine development [9]. Other adjuvant combinations have also been proposed for drug vaccine preparation, such as a mix of liposomes, MPLA and QS21 saponin forming a complex called AS01; an oil-in-water emulsion composed of α-tocopherol, squalene and polysorbate 80 (called AS03); lastly, AS04, which is an MPLA and aluminum hydroxide mix [9]. It should be mentioned the development of drug vaccines benefits considerably from other already in use or under approval adjuvants [31]. For example, a recent Food and Drug

Administration (FDA)-approved adjuvant MF59 used in influenza vaccines is a squalene oil-in-water emulsion that promotes B and T cells responses, which are important players in antibody generation [32,33].

Adjuvants or combinations have to be prepared specifically for immunogens to obtain the most favorable outcome; for example, oxycodone vaccine showed satisfactory results when tested with Freund's or alum adjuvants [20–22], but there was no outcome with MPLA [21]. Improvement in antibody production levels, affinity, binding capacity and efficacy in neutralizing the passage of nicotine molecules to the brain was shown during a combination of alum and CpG for developing a nicotine vaccine compared to the use of alum only [34,35]. In the same context, the addition of CpG to alum in a heroin vaccine preparation also remarkably improved the antibody titer and limited the antinociceptive effect of heroin [36,37]. From this, a combination of CpG with adjuvants ameliorates the specificity, antibody titer and effects of the vaccine, which consequently suggests the usefulness of this approach in drug vaccine improvement [30].

However, these potential combinations should be tested with different administration modes [21,37]. An approach of intradermal injection followed by laser activation that increases dendritic cells motility showed comparable results to those of intramuscular immunization of nicotine vaccine with alum, MPLA or MPLA/CpG [38]. Although, generally speaking, adjuvants are rated according to their efficacy, there are also the issues of toxicity, side effects and approval regulation. Therefore, great importance should be attributed to facilitating administration, decreasing cost, and making them user-friendly. This will also motivate researchers to further develop better ways, make use of already available or under approval adjuvants, and improve the existing vaccines for substance use disorders (Table 1).

2.2. *Cocaine*

Cocaine is rooted in modern society and its abuse keeps growing especially in third world countries. Many innocent lives are lost directly or indirectly because of drug consumption and drug market wars. Furthermore, since cocaine is mostly administered through injections, different infectious diseases, such as AIDS and hepatitis spread through users and non-users [39].

Cocaine is an enticing substance widely consumed for centuries by aboriginals of South America, where, according to customs, the coca leaves are chewed in order to facilitate working in high altitudes. Pure cocaine is easily smoked or ingested producing euphoric feelings and giving the user the impression that they are more effective and have greater strength. However, it is illegal and expensive, and its abuse often leads to crime and hinders the user to engage in an ordinary productive life. To date, no satisfactory medicinal procedure or approach has been found to prevent cocaine abuse [40,41].

People looking for treatment for their addiction are often offered vaccination combined with counseling. As described above, a good vaccine should have high antibody titer and affinity with fewer side effects. Cocaine offers multiple sites for linker attachment. For example, some ester or amide containing linkers (not changing structure or charge) are usually linked with the methyl ester group [42]. Some attached groups may influence the charge of the cocaine molecule. A carbon chain may subtly alter the charge while an amide or succinyl group removes its charge resulting in a reduction in the antibody binding capacity [43]. To date, KLH linking for vaccines is still being used on rodents to test the new approaches [7]. In human trials of cocaine vaccination, only one linker has been found effective from the different forms used on animals, which is recombinant cholera toxin B [7]. Research was able to determine the approximate concentration of cocaine in the blood after usage, as well as the anti-cocaine antibodies present in the bloodstream subsequent to vaccination [7,44]. From that process, in order to obtain better results, it is recommended that vaccination should be accompanied by counseling.

2.3. *Methamphetamine*

The abuse of methamphetamine is considered to be one of the most dreadful addictions because of its effects on the person's life and his surroundings. It is known as a strong drug since it has a longer half-life than cocaine. When metabolized, it produces amphetamine which is also a potent drug emphasizing the high addictive effect [7].

Illicit entrepreneurship has been built around the synthesis of this rather simple structured molecule. It can be produced from easily obtainable materials and simple tools. The addiction to methamphetamine has a wider range because of its easy availability on the streets in the ghettos where it is manufactured, compared to cocaine that predominates the urban areas.

Table 1 – Adjuvant-dependent immuno-conjugates.

Substance of abuse	Adjuvant	Carrier	Species	Ref.
Cocaine	Aluminium hydroxide	KLH	human	[72]
	Aluminium hydroxide	CTB	human	[73]
				[74]
	Ribi Adjuvant system	KLH	Rat	[75]
				[13]
	Complete/Incomplete Freund's adjuvant	BSA	mouse	[43]
Methamphetamine	Aluminium hydroxide (Alhydrogel)	Immunocyanin KLH	Rat	[25]
	Aluminum potassium Sulfate (alum)	KLH	Rat	[76]
	Ribi Adjuvant system	KLH	Mouse	[77]
	Ribi Adjuvant system	KLH	Rat	[24]

The fight against methamphetamine addiction through vaccine production lags behind the research being undertaken with other substances of abuse; however, this is not an exact reflection of the research interest toward methamphetamine. Currently, several groups have been developing vaccination strategies and producing monoclonal antibodies to methamphetamine and other byproducts [45,46]. These monoclonal antibodies are considered to be useful for overdose treatment and could potentially help in the treatment of addiction reduction. Vaccination research on rodents found a positive effect of the antibodies in reducing substance-related locomotor activity disturbance. Thus, it strongly suggested that vaccination could be a significant asset for addicts wishing to combat their addiction [7].

3. Recent detection methods

3.1. *Antibodies in drug detection*

Drug consumption for leisure purposes has become widespread, resulting in acute poisoning and possible death of the casual users. This situation has led to various organizations (such as the police) being very interested in substance use disorders detection methods in body fluids, especially the portable and on-site technologies [47].

Since the first hybridoma technology was first introduced in the 1970s, there has been a great increase in the use of antibodies as a tool for detection, prevention, and treatment, resulting in vaccine production, antigens detection, and characterization for genetic and immune response regulation completely reforming this field. The ability to produce monoclonal antibodies can be seen as a tremendous asset in a variety of fields such as diagnosis. It can be used for cancer and infectious diseases diagnosis but also in the detection of metabolic and abuse substances [47].

3.2. *Assays for substance use disorders*

By far, the gold standard method for the confirmation of substance use disorder in biological fluids is gas chromatography coupled with mass spectroscopy (GC–MS). In addition, other methods such as thin-layer chromatography (TLC), high-performance liquid chromatography (HPLC), and capillary electrophoresis (CE) are used for substance abuse detection [48]. GC–MS can only be performed after the sample has been screened through another technique for example immunoassay or TLC. Thus, chromatographic methods require heavy preparations and modified extractions which cannot be as readily available as the immunological based and the biosensors commercial kits.

3.2.1. *Immunoassays*

Antibodies occupy a prominent position in substance use disorders detection. They gave birth to many techniques, such as enzyme-linked immunosorbent assay (ELISA) [32], enzyme-multiplied immunoassay techniques (EMIT), fluorescence polarization immunoassays (FPIA), and up-converting phosphor technology (UPT) [48,49].

Immunoassays are either of a homogenous or heterogeneous type. The latter needs a separation between antigen-antibodies complexes from free antigens or antibodies by some kind of a solid support. ELISA sets an excellent example of such techniques. Depending on the characteristics of the used antibodies interaction with antigens, ELISA can be competitive or non-competitive (Fig. 2A); however, this separation is expendable for homogeneous immunoassays. Additionally, EMIT assays are based on the competitiveness of the labeled antibodies and antigens for drug abuse detection. A mixture of antibodies, labeled enzymes, and antigens (blood sample or urine containing drugs) will enter into a competition to interact with the antibody. The more antigens there are, the higher the enzyme activity can be seen (Fig. 2B). Many EMIT detection kits for cocaine and amphetamine can be found in the market [50]. Another example of detection is FPIA, which is based on the use of fluorescent substances interacting competitively with antigens and antibodies in solution (Fig. 2C). As before, a competition for the antibody will occur and the detection is performed through a vertically polarized detector. The detection is based on the difference of rotation between the free and the bound fluorescein-antigen. The free-form rotates at a higher speed resulting in a deviation of the incoming light that will not be detected, compared to the conjugate that is not able to rotate and thus the incoming light will not be diffracted and will be detected [50]. UPT differs from normal fluorescence, making use of lanthanide-containing ceramic particle emitting visible light after infrared absorption. It has no background auto-fluorescence making it a good means of creating detection strips based on colloidal gold or latex particles [49]. The phosphor molecules are chemically conjugated to antibodies and the principle of this test is based on competitiveness (Fig. 3). If drugs are not present in the biological sample, the UPT-antibody will diffuse and interact with the fixed protein giving a signal in the form of a line. However, in the drug-containing biological samples, the complex form (UPT-antibody-substance) is not going to interact with the fixed protein and gives no signal [49]. One of the standard assays is the agglutination assay based on the specific interaction between antigens and antibodies. When positive, it creates a visible agglutination, and over the years, different variations of this test have been seen, such as hemagglutination assay and latex agglutination assay. The Ontrak® kits produced by Roche diagnostics are a good example of substance detection kits in urine based on this principle [50].

3.2.2. *Biosensors*

Conventional approaches to drug use detection are typically chromatography, immunoassays, colorimetric assays, fluorescence and chemiluminescence methods and electrochemical sensors. From an analytical point of view, an ideal detection comes from the combination of chromatographic methodologies, such as high-performance liquid chromatography (HPLC) and gas chromatography-mass spectrometry (GC–MS) with other immunoassays; e.g., RIA and ELISA techniques. Although the performance of this combination is noteworthy, there are some drawbacks, such as long processing time and high cost, which encouraged the researchers

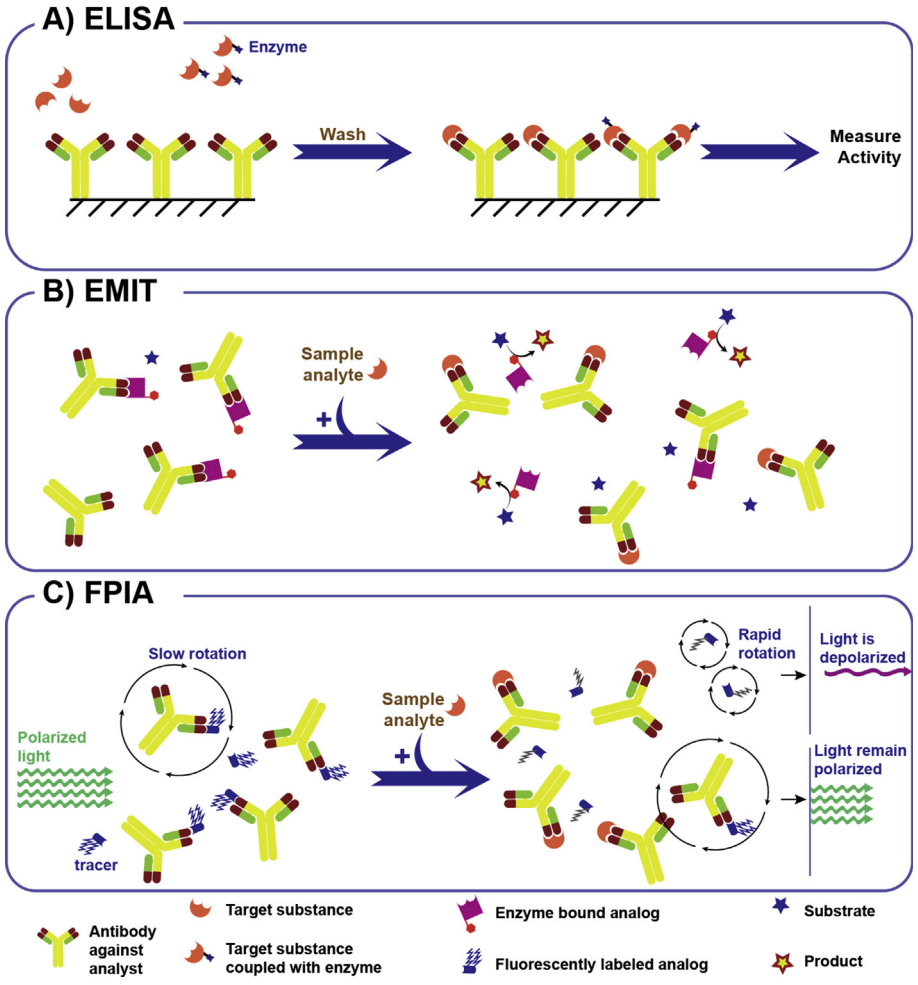

Fig. 2 – Overview of the most common immunoassays used in substance use analysis. (A) ELISA principle. (B) Enzyme multiplied immunoassay technique (EMIT). A substance-containing sample is put into competition with a labeled analog (with an enzyme such as glucose-6-phosphate dehydrogenase). The enzyme becomes inactive if the analog binds to the Ab. Thus, the signal generated from the enzymatic activity is lowered and is directly proportional to the substance concentration. (C) Fluorescence polarization immunoassay (FPIA) is also based on competition in addition to the polarized fluorescence-labeling signal. The principle is based on the Brownian motion generate. The free labeled-analogs affect the entering polarized light because of their rapid rotation. In contrast, fluorescent analogs bound to Abs become larger and a slow rotation is observed. Consequently, the polarized light is not affected, and the signal intensity is inversely proportional to substance concentration. Reproduced from Ref. [71] with permission under CC-BY license. © 2015 Sanavio and Krol. Frontiers Publishing.

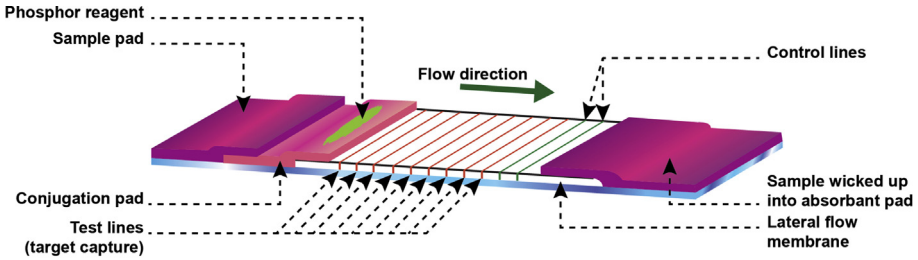

Fig. 3 – UPT lateral flow model. This detection format is used generally in strip manufacturing and is able to provide a dozen different test lines. Reproduced from Ref. [49] © 2001 Elsevier.

to develop novel detection/sensing technologies for better cost/performance systems [51]. From this situation, biosensors emerged with an enormous potential to support analytical applications. Biosensors are defined as a tool that integrates biologicals as a central part to implement its sensing properties. Some of these sensors are formed from whole cell biosensors, nucleic acid biosensors, aptasensors, immuno-sensors, peptides affinity sensors and polymer

biosensors; thus, it can be seen that immunology-based technology remains current [52].

Polymers conjugated to polypeptides are widely used in different bio-applications. Consequently, some of the conducting copolymers such as polythiophene-graft-polyphenylalanine (PT-*g*-PPhe) obtained by electrodeposition showed great potential as a sensor for substance use disorder detection [52]. Our group has been keenly interested in the utilization of novel polymeric architectures for the fabrication of biosensing platforms for illicit drug analysis. We have recently shown that electrochemically formed polythiophene bearing polyalanine homopeptide side chains (PT-PALA) was covalently conjugated with cocaine aptamer to form an aptasensor used for substance detection [53]. Furthermore, we have constructed a detection platform employing quantum dots (QDs) and gold nanoparticles (AuNPs) combined with aptamers that selectively identify cocaine and its metabolites. Poly-L-lysine coated μ-wells surfaces immobilizing QDs were then conjugated with AuNP-aptamers to form the bioanalysis system. The addition of either cocaine or its metabolite induces changes in the aptamer structure bound to the surface. Therefore, depending on the quantity of cocaine, fluorescence changes are observed due to the quenching effect of AuNP toward the fluorescence features of QDs [54]. In parallel, we established a novel detection platform for methamphetamine. The surface was based on a fluorescent-labeled polypeptide which was used to cover the electrodes in order to immobilize the methamphetamine selective antibody [52]. Recently, a double fluorescent μ-well cocaine assay, having a novel conjugated polymer containing cyclodextrin and polyethyleneglycol (PEG) as the key component was reported. In that design, the polymer itself exhibits fluorescence property, PEG and CD provide water solubility besides selective complexation with cocaine. In addition, cocaine antibody was used as a seconder recognition compound after labeling with QD. Therefore, selective cocaine binding was monitored by following two colors fluorescent signals [55].

3.2.3. *Commercial tests for drug detection*

Between 2003 and 2005, the European Union financed the ambitious project of ROSITA-2 (Roadside testing Assessment). It was implemented to screen the usability of on-site saliva testing devices for drug detection [47]. Different test kits were selected from various independent firms (see supplementary materials for more detail) for testing, and ultimately several of them failed in giving accurate results in regard to specificity, sample quality or technical readings. At the end of the project, no actual candidate was suggested as a reliable device for on-site detection, and this was due to various issues; for example, THC sensitivity. However, these limitations are being overturned step-by-step through the ongoing research [56,57]. In the meantime, urine and blood samples continue being the major source of detection and are completely implemented by law and fully accepted in the juridical institutions [58].

4. Technology-based prevention

Substance use disorders have a distinctive development process accompanied by many challenges that confront all the involved parties (*i.e.*, clinicians, patients, families and the community). The main challenge is that prevention and treatment are not sufficiently emphasized enough. A mere 5% of people with substance use disorders are aware of the magnitude of the issue [59]. Furthermore, the cost of prevention programs is constantly increasing due to the need to develop stronger and more optimal therapy and counseling approaches, which makes them more inaccessible for the low-income population [60]. Given the many prevention programs that offered positive results in research trials, only a limited number have been implemented to a wider extent. There is no full application of the programs due to the amount of human and financial resources that are required, and the need for staff training and securing special facilities [59].

Technology occupies an essential position in daily life. The wide access to tools like the internet, computers and mobile phones can be considered promising for assessment, educational prevention, wellness monitoring, and intervention for substance use disorders [61]. Technology-based programs for substance use disorder prevention are more appealing due to immediate availability to the patient, low development cost, elimination of human biases, reducing the need for training, and creating more flexible programs with central-made changes [62]. Furthermore, technology-based tools provide privacy for the individual, accessibility, convenience, and immediacy of the information, which enhances the motivation of the user and acceptance of change [62].

Much of the health software, websites and similar tools that support those with substance use disorders are readily available offering information, psychotherapeutic assistance, and various other functionalities [63]. Although the utilization of these instruments on mobile phones has generated a great deal of interest in terms of data gathering for research, there are many ethical issues of deep concern. From the positive perspective, portable devices with attachable sensors can be applied to an individual suspected of substance abuse to monitor the vital signs, such as heart rate, blood pressure, and substance concentration. This data can be transferred to clinicians to determine the situation and help prevent major relapse in the individual [64].

To raise the awareness of young people in relation to the dangers of substance abuse, many approaches have been implemented, such as academic programs, videos, and the internet to disseminate information. Many technology-based programs, such as “CLIMATE” or “Refuse to Use” have been created to prevent young people from becoming addicted to various substances (thoroughly reviewed here [65]). Research has shown that technology contributes greatly to the acquisition of knowledge and influences the behavior in adolescents and young adults [59]. However, it has been shown in a meta-analysis comparing face-to-face with technology-based interactions that there is no significant difference in efficiency between the two approaches [66].

It should be clarified that technology-based prevention, treatment or similar approaches are not attempts to replace the traditional therapy. Instead, they are intended to enrich the limited number of therapeutic approaches in treatment of substance abuse and prevention [67]. Technology-based programs are considered to be an alternative or to complement the traditional approaches. The interaction with the therapist

is still considered to be a fundamental component in the treatment of substance use disorders. However, the addition of technological tools into the equation should be taken as positive because it provides the opportunity to develop more effective clinical approaches and expand the therapeutic repertoire [68].

Interestingly, there is a paradoxical aspect of technology usage. Even though it can be used to innovate the current therapy and preventive approaches for substance use disorders, it may become a risk factor for drug use. Indeed, web-based tools and social media interaction can make it easier to access illicit substances [69,70].

5. Conclusion

Immunotherapy presents an interesting and innovative approach to drug abuse treatment and fighting addiction. Antibodies and vaccines products have presented exciting results with a good specificity to their respective drugs and expressed a significant potential in human treatment. Therefore, it should be reiterated that the utilization of such methods has a substantial impact on clinical applications and diagnosis. However, the visible drawbacks and the increase in the reckless use of drugs urged the responsible parties to develop different new approaches for detection (such as the use of biosensors). The production of on-site detection devices can be seen as a preventive way for traffic accidents, and street crime, thus contributing to the society. It should be noted that the treatment and prevention of substance use disorders are not infallible, however, their potential can be further displayed when supported by the continually developing technological tools.

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Appendix A. Supplementary data

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