IJPSR (2013), Vol. 4, Issue 4 **(Review Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 14 December, 2012; received in revised form, 15 January, 2013; accepted, 13 March, 2013

DRUG DELIVERY METHODS RANKING ADDICTION POTENTIAL

K. Sujatha*, T. Arundathi, S. Rubina, B.V. Ramana, G. Nagarajan

Department of Pharmaceutics, Dr. K.V. Subba Reddy Institute of Pharmacy, Dupadu, Kurnool, Andhra Pradesh, India

Keywords:
Abusers, Delivery Methods, Addiction, Awareness

Correspondence to Author:

K. Sujatha

Department of Pharmaceutics, Dr. K.V. Subba Reddy Institute of Pharmacy, Dupadu, Kurnool, Andhra Pradesh, India

E-mail: Ksujatha.bg@gmail.com

ABSTRACT: Substance abusers and drug addicts generally seek the fastest and most effective methods of getting high this means that drug delivery methods are important to users, and typically an addict will prefer one method over another. However, because there are a wide variety of drug delivery methods, substance abusers will often fluctuate between these techniques when the need arises. Understanding the different ways that people use drugs can aid in creating awareness and recognition skills to help combat drug abuse and addiction.

INTRODUCTION: Drug addiction is characterized by changes in the brain which result in a compulsive desire to use a drug. A combination of many factors including genetics, environment and behavior influence a person's addiction risk, making it an incredibly complicated disease. The new science of addiction considers all of these factors from biology to family to unravel the complexities of the addicted brain**.** This is explained by **figure 1**.

The research has shown that the faster a drug can reach the brain, the more likely it is to be addicting. Different methods of delivery-smoking, injecting, or snorting- largely influence how quickly a drug finds the brain. Delivery methods become an important factor when ranking the addiction potential of a drug [1]. This explained by **figure 2**.

QUICK RESPONSE CODE

IJPSR:
ICV (2011)- 5.07

Article can be accessed online on:
www.ijpsr.com

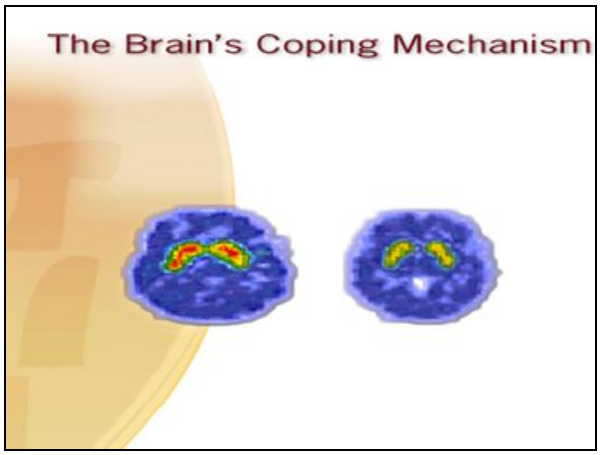

FIGURE 1: BRAIN'S COPING MECHANISM

Theory: The sap model is described by eq. (1.1):

$A = E/(tmax)(t_{1/2})$ ---------- (1.1)

In this model, a represents addictive potential in units of hr^{-2}, e represents euphoric potency on a scale from1 to 5 with 5 being the most potent, t1/2 (hr) is the elimination half-life and tmax(hr) is the time to peak absorption (rate of exposure) or time to peak concentration (extent of exposure) in plasma, blood or serum [2]. This is explained by **table 1, 2, 3**.

t_{max} is thus a hybrid pharmacokinetic parameter dependant on the fractional rate of drug absorption, (ka hr^{-1}), into body, as well as the fractional rate of drug elimination,(ke hr^{-1}), from the body

$$t_{max} = \ln(ka/ke)/(ka - ke) \text{---------- (1.2)}$$

The peak concentration, cmax is also a function of ka and ke.

$$C_{max} = kaF/d\ v_d\ (ka- ke)\ (\ e^{-keTmax}-e^{-KaTmax}) \text{-------(1.3)}$$

Where F (%) represents the bioavailability of the drug, d (mg) represents the oral dose administered, and vd represents its apparent volume of distribution. The half-life for the absorption process, defined as the time required for half the absorbed dose to be absorbed, is expressed as;

$$t_{1/2a} = \ln(2)\ /ka \text{---------- (1.4)}$$

where ln(2) =0.693. The $t_{1/2a}$ units are hours. Multiplying $t_{1/2a}$ by 5 to mark five half-lives to steady state gives the elapsed time equal to 96.875% of the absorbed dose (FD) which, for clinical purposes, represents complete absorption. Similarly, the half-life for the elimination process, expressed as [2];

$$t_{1/2} = \ln(2)/ke \text{----------(1.5)}$$

Multiplied by 5, represents complete elimination, thus, as shown by eqs. (1.4) and (1.5), ka and ke are "unconfounded" independent predictors of drug absorption and elimination, unlike the t_{max} in eq. (1.2**).**

TABLE 1: DRUGS RANKED BY THE SELARIAN RANKED POTENTIAL A

Rank	Drug	Intake Route
1.	Heroin	intravenous
2.	Cocaine	inhalation
3.	Alcohol	oral
4.	Morphine	intravenous
5.	Oxycontin	chewed
6.	Nicotine	inhalation
7.	Morphine	oral
8.	Oxycodone NR	oral
9.	Lorazepam	oral
10.	Oxycodone CR	oral
11.	Clonazepam	oral
12.	Amphetamine Salts	oral

TABLE 2: DRUGS RANKED BY THE LINARES ADDICTIVE POTENTIAL A_L

Rank	Drug	Intake Route
1	Heroin	intravenous
2	Concerta	oral
3	Methylphenidate	oral
4	Lisdexamphetamine	oral
5	Cocaine	inhalation
6	Alcohol	oral
7	Morphine	oral
8	Lorazepam	oral
9	Oxycodone NR	oral
10	Oxycodone CR	oral
11	Alprazolam	oral
12	Buprenorphine	oral
13	Clonazepam	oral
14	Morphine	intravenous
15	Amphetamine Salts	oral
16	Nicotine	inhalation
17	Methadone	oral
18	Diazepam	oral
19	Oxycontin	chewed
20	Dronabinol	oral
21	THC	inhalation

TABLE 3: GOLD STANDARD RANKS OF ADDICTIVE DRUGS

Gold Standard	FSKEO Rank
Heroin	1
Cocaine	2
Tobacco	3
Methadone	4
Alcohol	5
Benzodiazepines	6
Amphetamine	7
Cannabis	8
Methyl phenidate	9

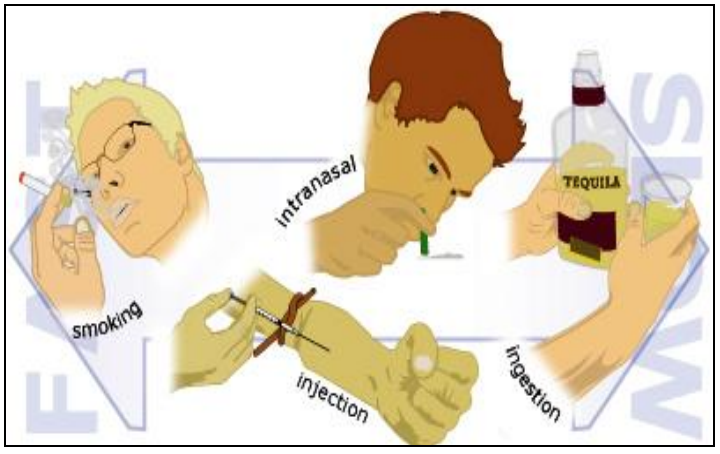

FIGURE 2: DRUG DELIVERY METHODS

Smoking-Methodology: Smoking drugs is widely considered to be the most effective method of getting high because the results are almost immediate.[3] This is a critical part of what drives people to use again and again the instant gratification, which is virtually synonymous with addictive behaviors according to the university of utah; drug users smoke drugs by causing them to combust in some way, this could be through a pipe, a piece of aluminum foil, a light bulb, rolled in a paper or rolled in a leaf.

In some cases substance abusers will put drugs on hot pieces of metal and suck the resulting fumes with a straw. Nearly anything can be outfitted to smoke drugs in this includes homemade pipes and bongs made from simple household items like toilet paper rolls, soda bottles, hoses, chunks of wood, apples, potatoes and many other makeshift smoking apparatus in nearly all cases users inhale the smoke release from a burning drug as deeply as possible, and then hold the "hit" as long as they can before slowly releasing it. Many addicts assume that by holding the smoke in their lungs for long periods of time that more of the psychoactive ingredients will be distributed in the blood stream.

Many types of drugs nearly every type of drug can be smoked, although not all combust at the same temperature for instance, very dry marijuana will combust at a much lower temperature than dense methamphetamine. Overall, the following drugs are often smoked, marijuana, opium, hash, cocaine, heroin, prescription medications, crack, PCP and a number of other designer drugs.

Risks: When a person inhales the smoke of anything drug or not they breathe in particulate material that can be irritating and dangerous to lung tissue. Over time consistent inhalation of smoke can cause serious lung disorders that in some cases can be fatal. This includes moderate afflictions like pneumonia or bronchitis, but it also includes serious diseases like lung, throat or mouth cancer, emphysema and cardiovascular disorders that can eventually lead to heart attack and stroke.

Additionally, smoking any substance regularly can cause premature aging and exacerbate existing dermatological problems like eczema, psoriasis and even allergies. Constant inhalation of smoke can affect the vocal chords by making a person's voice raspy and hoarse-sounding.

Smoking can cause substantial damage to the teeth, gums, jaw and tongue. Because smoking dehydrates the mouth, saliva that is critical for combating plague and periodontal disease will largely be absent and pave the way for painful dry pockets to form. Eventually this process can result in tooth decay, tooth loss and sometimes the need for a complete set of dentures – even though many addicts in this type of situation are often considered far too young to normally require such dental work. This is especially true in the case of heavy meth users, who are notorious for developing severe dental issues as just one of many consequences of their addiction.

Vaporizing- Methodology: Vaporizing sounds like something from a science fiction movie, but when it comes to drug abuse and addiction technology and science are rarely parts of the everyday illicit drug experience. However, vaporizing drugs is one of the first real instances of a high-tech drug delivery method that appears to work altogether too well for drug addicts.

In most cases people vaporize marijuana almost exclusively, although a number of other substances can be vaporized as well.[4] The primary perceived benefit of vaporizing a drug over smoking it is that by vaporizing it, a person is essentially inhaling water vapor with psychoactive properties. This is because vaporizers superheat the air around a drug – always remaining at temperatures less than the combustion point for that substance when the air around a substance is superheated it causes all of the moisture in the substance to escape rapidly. That moisture escapes in the form of water vapor that drug users inhale as if it were smoke.

However, because there is no smoke involved there are fewer – if any – dangerous carcinogenic particulates being breathed into the lungs. Therefore, substance abusers rationalize that vaporizing a drug must be healthier than smoking it. In a comprehensive online study into the matter, evidence strongly pointed to the idea that vaporizing is indeed a healthier drug delivery method than smoking. In a paper on the matter for the national center for biotechnology information, mitch early wine and sara smucker barnwell. "A significant interaction revealed that the impact of a vaporizer was larger as the amount of cannabis used increased. These data suggest that the safety of cannabis can increase with the use of a vaporizer.

Regular users of joints, blunts, pipes, and water pipes might decrease respiratory symptoms by switching to a vaporizer."

Types of drugs: Most people use vaporizers strictly for smoking marijuana flower buds, stems and leaves. However, nearly any drug that has moisture content can be vaporized, although there are few if any reports available about the effects of vaporizing substances other than marijuana.

Risks: While vaporizing a substance is probably less dangerous than smoking it, there is still a great deal about vaporizing that is unknown. This drug delivery method has increased in popularity only in recent years and no credible studies have been conducted into the matter to date. In drug delivery methods part 2 we'll discuss the other major ways that drug users consume their substances of choice[5]. This includes snorting or insufflation, absorption, ingestion, inhalation and injection.

Absorption-Methodology: Absorption was a drug delivery method popularized by jimmy Hendrix, despite the fact that humans have been using this practice for thousands of years to achieve an altered state of consciousness. Hendrix accomplished this by allegedly placing LSD on his forehead and letting it absorb through his skin. Rumors have maintained for decades that this was the reason for the guitarist's constant use of a bandana wrapped around his forehead.

Reports of this transdermal property are likely true considering that the first known use of LSD occurred when a swiss scientist accidentally handled the substance and subsequently embarked on the first known LSD "trip." Albert Hoffman, the creator of lysergic acid diethylamide, recounted his first experience with the drug, which he apparently absorbed through his skin; "because of the known toxicity of ergot substances, I always maintained meticulously neat work habits.

Possibly a bit of the LSD solution had contacted my fingertips during crystallization, and a trace of the substance was absorbed through the skin. If LSD-25 had indeed been the cause of this bizarre experience, then it must be a substance of extraordinary potency." [6,7,8] But LSD isn't the only drug that can be administered trans-dermally.

Illicit substances can be absorbed through nearly any part of the skin, or it can be dissolved in mucous membranes like the mouth, eyes, and even in the anus. (although technically this last method is considered more "ingestion," than anything, despite the fact that the drugs are absorbed into the bloodstream by the colon. in fact, the absorption method is how products like nicotine or pain-reliever patches work they release a small amount of the required substance slowly into the skin. and while this might not be a preferred method by most drug users, it does tend to have more consistent and longer lasting effects than other drug delivery methods.

Types of drugs: When prepared in the correct manner nearly any type of drug can be administered with a transdermal application. This includes drug patches already widely prescribed – and diverted by drug addicts – such as fentanyl, methadone, morphine and many others. Illicit drugs that some users regularly handle like cocaine, heroin, meth, crack, ecstasy and ketamine can also be absorbed through the skin if the contact is frequent enough and the drugs are of high potency.

Risks: Few studies have been conducted to determine if the risks of trans-dermal drug administration are any more or less significant than the risks of other drug delivery methods. However, because the effects take much longer to take effect, some substance abusers can place themselves at risk of overdose when they apply more than necessary because they do not feel immediate results.

Injection-Methodology: Intravenous drug use is by far the most dangerous of all types of drug delivery methods and is likely responsible for more overdoses than any other type. This drug delivery method requires the use of hypodermic needles to inject illicit substances directly into the veins and therefore the bloodstream, where the drugs will have a direct path to the brain.

Many intravenous drug users carry complete kits with them that include tourniquets, needles, syringes, rags, tubes, lighters, a spoon, and other IV drug use items. Because needles are highly regulated in the U.S., many drug users are forced to reuse the same needles over and over again. Injections cause small to moderate injuries depending on the user's abilities and experience with needles.

This means that over time, "track marks" can build up in an area that an addict uses regularly for injections. therefore, many addicts will inject into difficult-to-spot areas like in between the toes, in the scalp, the buttocks and even on the inside of the lips injections can also be administered intramuscularly, which involves placing the needle deep into a large group of muscles and injecting the substance directly into it, where the muscles will then absorb the drug into the bloodstream.

Types of drugs: Opiates are commonly injected, including prescription drugs like oxycontin that are "cooked down" into a solution and placed in a syringe. Cocaine, meth, ketamine, morphine and other drugs can also be injected. However, the most widely injected drug is heroin and other versions of heroin like methadone.

Risks: From the risk of infectious disease like hepatitis, HIV and other life-threatening diseases to the significant risk of overdose, this drug delivery method is by far the most dangerous. Additionally, intravenous drug use is also associated with a high risk of violence, rape, murder and suicide. IV drug use leads to addiction rapidly, and relapse rates among people that attempt to stop using are astonishingly high.

However, blood-borne illnesses present the most significant threat [9, 10]. According to Jim Davis, founder of recovery first, a powerful drug rehabcenter; "blood borne illnesses of any type are always a risk when sharing needles or using needles in an unsanitary manner. Hepatitis c (and other versions of the virus) is a dangerous disease of the liver that is directly associated with idus. This is a non-curable illness . . ."

Inhalation-Methodology: Inhalation is not to be confused with insufflation or snorting. Whereas the latter consists of the act of snorting an actual physical substance into the nasal and sinus passages, inhalation deals with vapors only [11].

These often consist of the vapors of various liquids that give off gases when exposed to the air. In most cases users will breathe these substances directly from the container they are in, or they'll soak a rag or other cloth in the substance and breathe through the rag.

Types of drugs: Most of these drugs consist of common household products like furniture polish, potpourri spray, gasoline, permanent markers and so on. However, some illicit drugs, such as the drug known as rush, are only marketed to black market drug users and have no known applications other than intoxication.

Risks: The risks of inhaling certain chemical vapors can be deadly – especially when the drugs in question are household products that were never meant for human consumption. According to the anti drug, an organization dedicated to educating people about the effects of drug use, states; "sniffing highly concentrated amounts of the chemicals in solvents or aerosol sprays can directly induce heart failure and death.

Heart failure results from the chemicals interfering with the heart's rhythm regulating system, causing the heart to stop beating. This is especially common from the abuse of fluorocarbons and butane-type gases.

High concentrations of inhalants also cause death from asphyxiation, suffocation, convulsions or seizures, coma, choking or fatal injury from accidents while intoxicated." Regardless of the delivery method, all drugs can be dangerous – and some can be deadly.

Addiction and the threat of serious legal consequences including prison time are all very real possibilitiesof the risks [12, 13, 14]. The fastest way to get a drug to the brain is by smoking it. When a drug like tobacco smoke is taken into the lungs, nicotine (the addictive chemical in tobacco) seeps into lung blood where it can quickly travel to the brain. This fast delivery is one reason smoking cigarettes is so addicting.

Injecting a drug directly into a blood vessel is the second fastest way to get a drug to the brain, followed by snorting or sniffing it through the nose. The slowest mode of delivery is by ingestion, such as drinking alcohol.

The effects of alcohol take many minutes rather than a few seconds to cause behavioral and biological changes in the brain

Rapid Delivery Changes in Brain: Nobody likes to wait, so users often choose a delivery method that gets them higher, faster. As addiction progresses, users often seek out the more immediate and more intense high.[15] But this doesn't seem to be the only reason that rapid delivery is an important factor in addiction[16]. Recent evidence suggests that the mode of delivery can actually influence which part of the brain is most affected by a drug. Rapid delivery, such as smoking, affects brain regions that facilitate addiction. This is explained by **figure 3**.

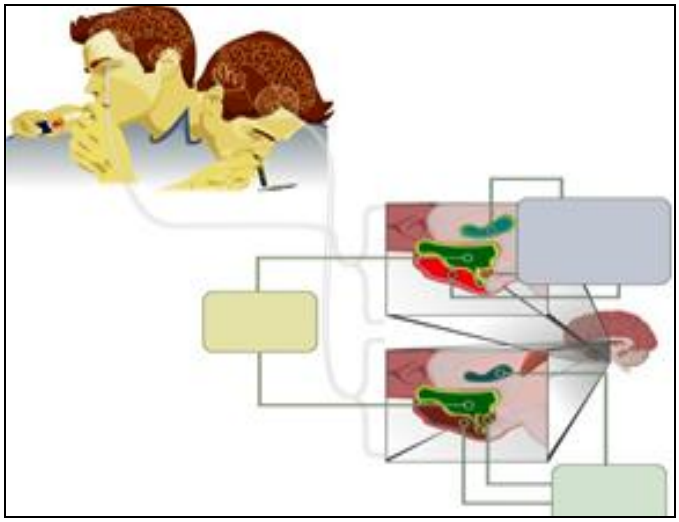

FIGURE 3: FASTEST DELIVERY TO BRAIN

Slow Delivery an Addiction Therapy: Increased knowledge about drug delivery methods is leading to new addiction therapies. It turns out that delivering a drug slowly, by ingestion or through the skin, produces a weaker, longer-lasting effect.[17,18] Slow delivery allows the drug to temporarily stabilize the brain and help reduce withdrawal symptoms over a longer period of time. And slow delivery is less addicting! So it's becoming an increasingly popular treatment option. This is explained by **figure 4**.

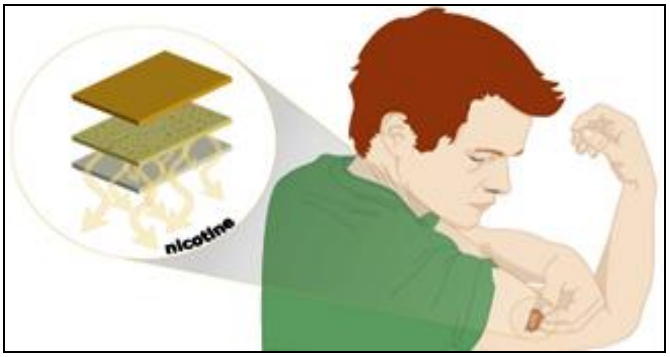

FIGURE 4: A PATCH PLACED ON THE SKIN IS USED TO SLOWLY DELIVER NICOTINE TO A SMOKER TRYING TO QUIT.

CONCLUSION: Early use and later problematic use are risk factors for future delinquency numerous studies have documented the strong link between alcohol and drug consumption and crime. Prevention programs successful in reducing and/or preventing the number of individuals who abuse alcohol and drugs contribute to reductions in later delinquency.

FUTURE DIRECTIONS: Salient future directions involve accounting for inter individual differences in addictive potential. The LMM is a not an individual-specific model. For example, the model cannot account for individual-specific genetic and psychosocial influences affecting addiction. In addition, the model does not take into account individual pharmacokinetic traits that may predispose a particular individual, more than another, to opioid addiction.

REFERENCES:

1. Gibaldi, M., Perrier, D., Marcel Decker, a text book of Pharmacokinetics. New York. 1975.
2. Salerian, A. Addictive potential: $A = E/T_{max} \times t_{1/2}$,Med Hypotheses 2010,74;1081-1083.
3. Bigelow and preston,drug discrimination methods for drug characterization Nida research
4. Bozarth, and wise, intracranial self-administration of morphine into the ventral lif sciences 1981, 28: 551-555.
5. Fowler JS, Logan J, Wang G-J, Volkow andmonoamine oxidase and cigarette smoking. neurotoxicology 2003; 24: 75–82.
6. Liebman, J.M., and Cooper, S.J. (eds.), the neuro pharmacological basis of reward newyork, ny: claredon press, 1989.
7. Sayette MA, Shiffman S, Tiffany ST, Niaura RS, Martin CS, Shadel wg the measurement of drug craving. addiction 2000; 95, 189–210.
8. Henningfield JE, Keenan R Nicotine delivery kinetics and abuse liability. J Consult Clin Psychol 1993; 61: 743–50.
9. Pepe, M., Longton, G. Standardizing markers to evaluate and compare their performances. Epidemiology.
10. Khoo, K., Gibaldi, M., Brazzell, R. Comparison of statistical moment parameters to Cmax and Tmax for detecting differences in *in vivo* dissolution rates. J Pharm Sci. 1985 , 1340-1342.
11. Linares, O., Jacquez, J., Zech, L., Smith, M., Sanfield, J., Morrow, L., Rosen, S., Halter, J. Norepinephrine metabolism in humans: kinetic analysis and model. J Clin Investig. 1987, 80, 1332-1341.
12. Hagdu, A., Dendukuri, N., Hilden, J. Evaluation of nucleic acid amplification tests in the absence of a perfect gold-standard test: a review of the statistical and epidemiologic issues. Epidemiology 2005, 16, 604-612.

13. Daly, A., Linares, O., Smith, M., Starling, M., Supiano, M. Dobutamine pharmacokinetics during dobutamine stress echocardiography. Am J Cardiol. 79, 1381-1386
14. Akaike, H. A new look at the statistical model identification. IEEE Trans Automat Contr. 1974;19, 716-723.
15. Nutt, D., King, L., Saulsbury, W., Blakemore, C. Development of a rational scale to asses the harm of drugs of potential misuse. Lancet 2008; 369, 1047-1053.
16. Koob, g. F., and Bloom, F. E., "Cellular and molecular mechanisms of drug dependence,"Science1988 ; 242:715-723,
17. Iffany ST, Drobes DJ. The development and initial validation of a questionnaire on smoking urges. br j addict 1991;86:1467–76.
18. O'brien CP. Anticraving medications for relapse prevention: a possible new class of psychoactive medications. am j psychiatry 2005;162:1423–31.

How to cite this article:
Sujatha K, Arundathi T, Rubina S, Ramana BV, Nagarajan G: Drug Delivery Methods Ranking Addiction Potential. *Int J Pharm Sci Res* 2013; 4(4); 1287-1293.