



## CAUTION: MEDICINES CAN KILL, BEWARE

Anoop Paruchuri<sup>1</sup>, Vini P<sup>1</sup>, Akram Ahmad<sup>1\*</sup>, Selvamuthu Kumaran S<sup>2</sup>, Mohanta G P<sup>1</sup>, Manna P K<sup>1</sup>

<sup>1</sup>Department of Pharmacy Practice, Annamalai University, Annamali Nagar-608002. Tamilnadu.

<sup>2</sup>Department of Medicine, RMMC&H, Annamalai Nagar-608002. Tamilnadu. India.

Email: [akrampharma67@gmail.com](mailto:akrampharma67@gmail.com)

**ABSTRACT:** A drug is one which includes "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals" and "articles (other than food) intended to affect the structure or any function of the body of man or other animals". Taking the right drug in right amount at a right time literally gives us a second chance to live. Medicines are the greatest man made resources which help in recuperation. But if you were paying close attention the news for the last decade you can find out these same drugs killed many of the celebrities we admired. From yester years Marlin Monroe to the yesterday's Michael Jackson the reason was the same. Either by intention or accident they consumed large doses of the drug prescribed for their specific illness. One good thing about these medicines is they do their role when taken in prescribed amount but, once they are overdosed they cause most grievous complications and may be even death. There is thing circulating in the medical field that TB (Tuberculosis) is a poor man's disease and CCF (congestive cardiac failure) is a rich man's disease, but to these drugs there is no such discrimination. No matter how you are or what you are you misuse them you pay the price eventually. The death of these celebrities should be adequate enough for us to respect their side effects but on the contrary these precious resources are considered to be a curse. Proper patient and community education should be done so that the person who is taking it is totally reminiscent of its side effects and risk on overdosing. This eventually helps us to fight the diseases better and obtain supreme benefit from the limited resources we got.

**KEY WORDS:** Michael Jackson, Propofol, Celebrity death.

### INTRODUCTION

A drug is defined as that which includes "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals" and "articles (other than food) intended to affect the structure or any function of the body of man or other animals"<sup>[1]</sup>. A great chemist once said "Poisons in small doses are best medicines and useful medicines in large doses are poisons"<sup>[2]</sup> also the similar thing is emphasized by a Swiss physician and chemist *Paracelsus* nearly 500 years ago that "All substances are poison; there is not which is not a poison"<sup>[2]</sup> which means any drug though it is useful it can become a potent poison if it precedes the required range. Drug induced toxicity can also occur from potential drug interactions between drugs, drugs and food. So it is required to understand proper pharmacology before

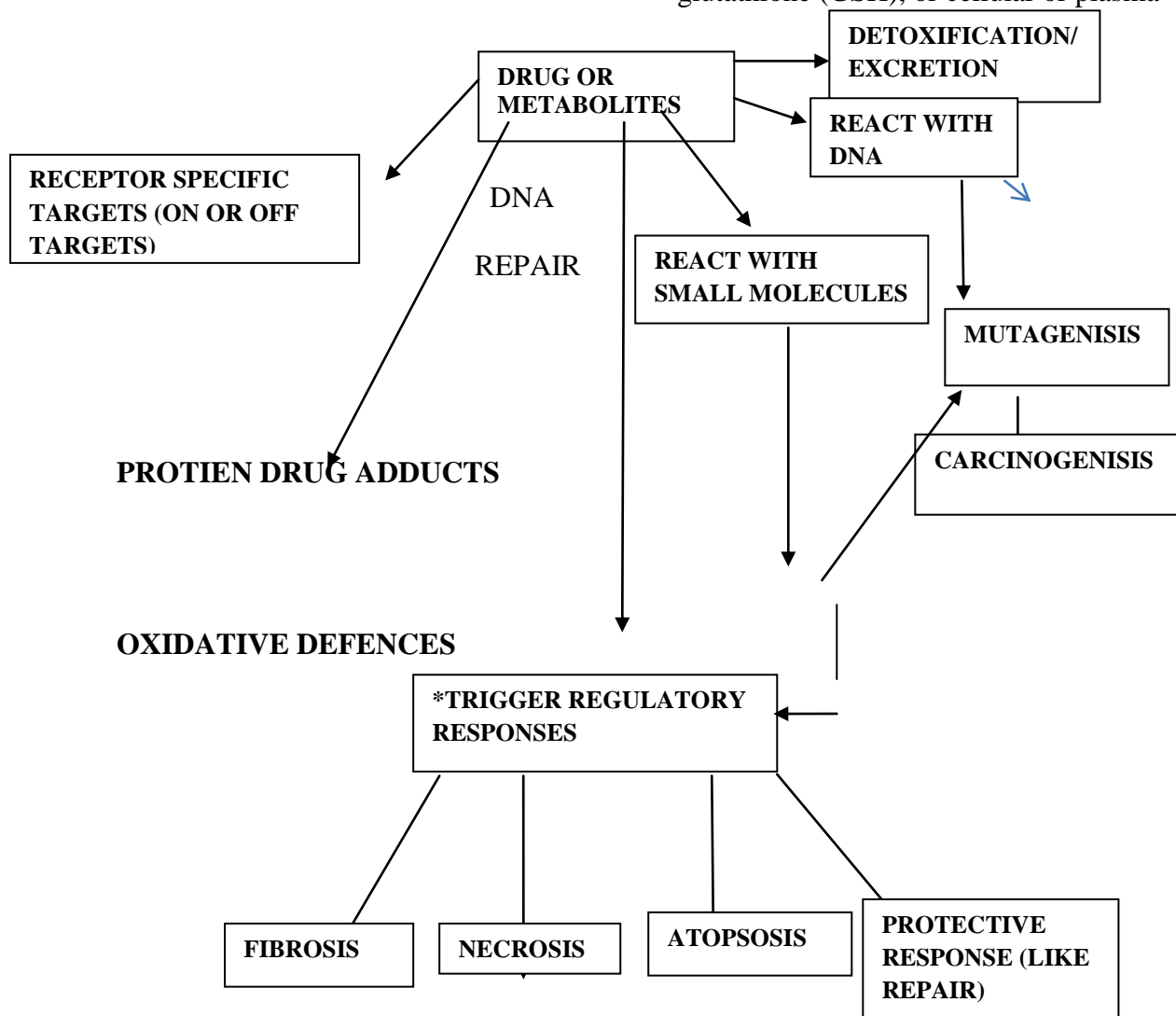
prescribing any drug and it is the responsibility of the patient to follow the instructions given by their physicians.

### PHARMACOLOGY

Even though the drug toxicity was discovered by the Greek almost in the late 18<sup>th</sup> century but the actual mechanism was studied only in the 20<sup>th</sup> century<sup>[2]</sup>. Different mechanisms of drug overdose toxicity were proposed but the widely accepted mechanism include on target and off target mechanisms<sup>[2, 3]</sup>.



can react with a variety of macromolecules including DNA, small antioxidants such as glutathione (GSH), or cellular or plasma



Drug when consumed reaches the blood in order to exert its pharmacological actions. The concentration of the drug in the blood is called serum plasma concentration which is a direct measure of its pharmacokinetics. For every drug there is a specific plasma concentration range below which the drug is ineffective and above which the drug becomes toxic. Most of the drugs taken orally are metabolized in liver and a few in kidney forming drug metabolites [3, 4]. A drug or its metabolites or both interact with specific receptors to mediate on-target or off target adverse effects. In addition, metabolites can be detoxified and excreted, or

proteins. The formation of unrepaired DNA adducts is often mutagenic and may lead to cancer. The impairment of oxidative defenses can lead to inflammation and cell death (apoptosis or necrosis). The formation of drug-protein adducts can trigger immune responses that can damage cells and tissues. Regardless of the mechanism of damage, a gradation of acute responses from protective to apoptosis and necrosis can result, depending on the extent of damage and the temporal and dose relationships. Chronic inflammation and repair can also lead to tissue fibrosis [5, 6, 7]. Our body



responds to drug overdosing by \*Trigger regulatory response which is all/ one of the following<sup>[4]</sup>:

**Necrosis** is enzymatic digestion of cellular contents, denaturation of cellular proteins, and disruption of cellular membranes.

**Apoptosis** is programmed cell death.

**Carcinogenesis** is the transformation of a normal cell into a neoplastic cell.

A **carcinogen** is a chemical, physical, or biologic insult that acts by causing DNA damage (mutations).

**Fibrosis** is the extensive deposition of collagen and fibrous material due to excessive cellular damage.

The above process stands true for recreational drugs (Marijuana), prescription drugs (Opiates) or OTC drugs (Paracetamol).

## SYMPTOMS<sup>[8]</sup>

Drug overdose symptoms vary widely depending on the specific drug used, but may include:

- Abnormal pupil size
- Agitation
- Convulsions
- Death
- Delusional or paranoid behavior
- Difficulty breathing
- Drowsiness
- Hallucinations
- Nausea and vomiting
- Nonreactive pupils (pupils that do not change size when exposed to light)
- Staggering or unsteady gait (ataxia)
- Sweating or extremely dry, hot skin
- Tremors
- Unconsciousness (coma)
- Violent or aggressive behavior.

**TREATMENT<sup>[8]</sup>**:The following should be done when a drug overdose is observed though intentional or unintentional.

1. Check the patient's airway, breathing, and pulse. If necessary, begin CAB i.e. circulation airway and breathing if the patient is unconscious but breathing, carefully place him or her in the recovery position. If the patient is

conscious, loosen the clothing, keep the person warm, and provide reassurance. Try to keep the patient calm. If an overdose is suspected, try to prevent the patient from taking more drugs. Call for immediate medical assistance.

2. Treat the patient for signs of shock, if necessary. Signs include: weakness, bluish lips and fingernails, clammy skin, paleness, and decreasing alertness.

3. If the patient is having seizures, give convulsion first aid.

4. Keep monitoring the patient's vital signs (pulse, rate of breathing, blood pressure) until emergency medical help arrives.

5. If possible, try to determine which drug(s) were taken and when. Save any available pill bottles or other drug containers. Provide this information to emergency medical personnel.

## DO NOT

- Do NOT jeopardize your own safety. Some drugs can cause violent and unpredictable behavior. Call for professional assistance.
- Do NOT try to reason with someone who is on drugs. Do not expect them to behave reasonably.

Do NOT offer your opinions when giving help. You do not need to know why drugs were taken in order to give effective first aid. The entire above are only temporary measures to save the patient from death, A permanent self-realization should come within which prevents this drug toxicity. Patients taking multiple drugs, pediatrics and geriatrics the care giver should be properly explained about pros and cons of the medicines.

## WHAT EXACTLY HAPPENED IN CASE OF MICHAEL JACKSON?<sup>[9,10,11]</sup>

**Source:**<http://images.mirror.co.uk/upl/m4/oct2011/6/6/michael-jackson-image-3-817923926.jpg>

Michael Joseph Jackson (August 29 1958 – 25 June 2009) aka King of Pop and M. J born in Gary, Indiana was a renowned rock star who doesn't need any introduction. He rocked the world with his music for several decades and was number one on the charts for a long time.



As it is the law of life that one should face difficulties at least at one point of time and even this rock star was no exception. It all happened in 1984 while filming a commercial for Pepsi where his hair caught on fire which he burned his scalp so bad that he had to be on painkillers and sedatives to ease his pain. He was on Diazepam, Lorazepam and Midazolam, where most of them were injected eventually led him to their addiction. So on the night of his death the regular sedatives failed in sedating him as he developed resistance towards them, he allegedly asked his doctor to give him Milk (Propofol, a very potential sedative which M.J. nicknamed 'Milk'). So his physician gave him 25 milligrams (an empty 100ml vial was found in his room during an investigation) of "Propofol" (marketed as Diprivan in the US) diluted with Lidocaine which made him sleep to eternity. It's illegal in the US even for a physician to use this drug in his normal In/ Outpatient setting. The autopsy reports confirmed the death due to Propofol intoxication and also reported that the contributing effect was by two other sedatives Lorazepam and Midazolam which were also found in M.J.'s blood stream. M.J. was officially announced dead on June 25, 2009 at 2:06 pm. In Los Angeles on 7 November 2011, the physician (Dr. Conrad Murray) was charged guilty for possession and use of the drug in a non-emergency setting and was sentenced to jail for 4 years along with the termination of his medical degree [12]. Source of the above images: References from 9-12.

**THE DRUG** [9, 10, 13, 14]: Propofol is an intravenous anesthetic agent which is used only in the emergency setting. It is a phenol derivative anesthetic with a pregnancy risk factor as "B" and listed as Schedule "H" in India [15] and "IV" in the US [16]. It is contraindicated in children under 16 receiving intensive therapy. The recommended dose of this drug in adults is 1-25mg/kg of 1% solution at the rate 20-30mg every 10 seconds until response is achieved. The maintenance

dose is 4-12mg/kg/hour I.V. [17]. The drug is so classified that even a physician cannot prescribe to his patients. The drug was strictly restricted to the emergency rooms where the patient needs to be sedated fast so that an emergency procedure can be performed. This drug is highly lipophilic which makes it enter the CNS and exert its action in less than 5 minutes. The toxicity range for the drug is so narrow that if not monitored the patient goes into respiratory depression. In a non-scientific explanation "This drug makes the brain to sleep and it does such a way that the brain forgets to breathe eventually causing death". Once a patient quits breathing, the body switches to anaerobic metabolism, lactic acid levels build, and organs quickly fail. This mechanism makes the drug odd man out among all the regularly used sedatives limiting its use only to an emergency setting. So when this was given to M.J., he passed into respiratory depression and as there was no proper equipment like in the I.C.U. available at home, the doctor couldn't do anything except watch him die.

\*- Substances in this schedule have a low potential for abuse relative to substances in schedule I, II and III.

\*\*- Schedule H includes all the injectable, antibiotics and prescription drugs.

#- Animal studies haven't shown an adverse effect on the fetus but no adequate clinical studies in pregnant women.

In India the drug is available under the following brand names [18]

BRAND NAME	MANUFACTURER	PRICE (INR)
Critifol	AHPL	104.16 (1% 12ml vial)
Diprivan Injection	AHPL	384.64 (2% 20ml vial)
Hypro	CelonPharma	126.00



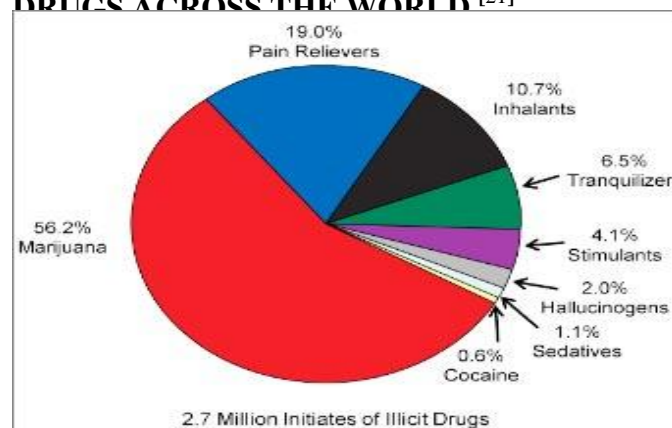
		(100mg tablet)
Propovan	Bharat Serum	84.00 (1% 10ml vial)

### FEW OTHER CELEBS KILLED ON DRUG ABUSE/ OVERDOSING. <sup>[19, 20]</sup>

NAME	DIED IN	DRUG RESPONSIBLE
Amy Wine house (Singer)	2011	Alcohol Poisoning.
Umaga (Wrestler)	2009	Acute toxicity due to combined effects of Hydrocodone, Carisoprodol, and Diazepam
Andrew Martin, aka Test (Wrestler)	2009	Oxycodone overdose
Heath Ledger (Actor. Well known as Joker from the last Bat Man movie.)	2008	Painkillers Oxycodone And Hydrocodone, Sleep Aid Temazepam And Sedatives Diazepam, Alprazolam And Doxylamine.
Natasha Collins (Actress)	2008	Cocaine Overdose
Pimp C (Rapper)	2007	Codeine and Promethazine
Anna N Smith (Actress)	2006	Clonazepam, Chloral Hydrate and Oxazepam
Eddie Gurrero (Wrestler)	2005	Heart disease, complicated by an enlarged heart resulting from a history of anabolic steroid

		use
Elvis Presley (Legendary Rock Star)	1977	As Many As 14 Different Drugs, Including Codeine And Methaqualone
Bruce Lee (Actor)	1976	Equagesic (Pain Killer)
Guru Dutt (Actor)	1964	Overdose of sleeping pills with alcohol.
Marilyn Monroe (Actress)	1962	Phenobarbital and Chloral hydrate
Sigmund Freud (Neurologist)	1939	Physician assisted Morphine overdose.

### COMMONLY ABUSED/ OVERDOSED DRUGS ACROSS THE WORLD <sup>[21]</sup>



### CONCLUSION

The death of M.J. casted a false image on Propofol leading to its rejection by many of the patients about to undergo a surgery. In fact Propofol is a wonderful anesthetic but was used in an inappropriate setting. The outcome of a perfect treatment depends on the three main basic principles which are "Right Drug, in Right Amount at a Right time". Anyone who overlooks the above principles will pay the price one way or the other. Drug abuse among the youth has become a rising tide in



the country. The sale of the prescription drugs without a prescription has also increased as there is no proper monitoring in the country. Tight monitoring both by the state and central regulatory authority should be done and a proper patient education should be practiced by the physician and the pharmacist. As it is laid down by the law that suicide is a crime, people who commit suicide and fail must be subjected to intense punishment which prevents others or the same person from repetition. Recreational drugs are widely used in the "Rave Parties" mostly in the metros, where the youth comes into contact with the drugs. This eventually leads to physical and psychological dependence which drives them to take high doses or shift to more potential drugs. Proper community education and monitoring should be enforced by the government which reduces the risk of overdosing and potential for drug abuse. A proper protocol should be laid down to prevent drug related deaths and to exercise rational drug use only through which maximum benefits can be reaped from our limited resources.

## REFERENCES

1. Federal Food, Drug, and Cosmetic Act. U.S Food and drug administration. Drug safety information [online]. 2011 [updated 2011 September 8]. Available from: <http://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm165107.htm>
2. Daniel C. Liebler & F. Peter Guengerich. Elucidating Mechanism of Drug Toxicity [online]. 2011 [cited 2005 May]. Available from: [www.cdc.gov/HomeandRecreationalSafety/pubs/RXReport\\_web-a.pdf](http://www.cdc.gov/HomeandRecreationalSafety/pubs/RXReport_web-a.pdf)
3. Cullen M. Taniguchi et al. Fundamental Principles of Pharmacology. 3<sup>rd</sup> edition; 2007.
4. Jean-Maurice Vergnaud, Iosif-Daniel Rosca. Assessing Bioavailability of Drug Delivery Systems. Florida; CRC press. 2005.
5. Tripathi K D. Essentials of Medical Pharmacology. 6<sup>th</sup> ed. New Delhi; Jaypee brothers. 2008.
6. John J Fenton, editor. Clinical Toxicology (A case related approach). U.S.A: CRC press; 2002.
7. Houck KA, Kavlock RJ. Understanding mechanisms of toxicity: insights from drug discovery research [online]. 2011 [cited 2007 November 4]. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/18063003>
8. Medicine Plus. Drug Abuse First Aid [online]. 2011 [updated 2010 September 6]. Available from: <http://www.nlm.nih.gov/medlineplus/ency/article/000016.htm>
9. Benjamin C. Wedro. Medicine net. Michael Jackson's Death [online]. 2011 [cited 2011]. Available from: <http://www.medicinenet.com/script/main/art.asp?articlekey=113188>
10. India Today. Michael Jackson's Physician Admits Giving Propofol to singer (online). 2011 [updated 2011 December 2]. Available from: <http://indiatoday.intoday.in/story/physician-admits-giving-propofol-to-michael-jackson/1/154222.html>
11. Michael Jackson's death. ABC news (online). 2011 [cited 2011 September 27]. Available from: <http://abcnews.go.com/US/michael-jackson-death-trial-kenny-ortega-worried-mjs/story?id=14614384>
12. Conrad Murray found guilty in Michael Jackson trial. CNN (online). 2011 [cited 2011 November 7]. Available from: [http://articles.cnn.com/2011-11-07/justice/justice\\_california-conrad-](http://articles.cnn.com/2011-11-07/justice/justice_california-conrad-)



- murray-trial\_1\_surgical-anesthetic-propofol-defense-attorney-ed-  
chernoff-conrad-  
murray?\_s=PM:JUSTICE
13. Micromedex Health Care Series. Thomson Reuters. U.S.A; 2011. Volume 149.
  14. Sean C Sweet man, editor. Martindale the complete drug reference. 36<sup>th</sup>ed. London: Pharmaceutical Press; 2009.
  15. Schedule H Drugs. Drugs and Cosmetics Rules. Ministry of Health and Family Welfare [Online]. 2011 [cited 2006 March]. Available from: [http://www.drugscontrol.org/Schedule\\_H.pdf](http://www.drugscontrol.org/Schedule_H.pdf)
  16. Controlled Substance Schedules. U.S department of Justice and Drug Enforcement Division [online]. 2011 [updated 2011 November]. Available from: <http://www.deadiversion.usdoj.gov/schedules/index.html>
  17. British National Formulary. 61<sup>st</sup> edition. London: Royal Pharmaceutical society; March; 2011.
  18. Monica Bhatia, Publisher. Current Index of Medical Specialties (CIMS). 113<sup>th</sup> ed. UBM Medica; April- July, 2011.
  19. List of Drug related deaths [online]. 2011. Available from [http://en.wikipedia.org/wiki/List\\_of\\_drug-related\\_deaths](http://en.wikipedia.org/wiki/List_of_drug-related_deaths).
  20. Celebrities died from prescription death [online]. 2011. Available from: <http://www.pharmacytechs.net/blog/18-celebrities-who-died-from-prescription-drugs>.
  21. Drug related celebrity deaths [online]. 2011. Available from: <http://www.pharmaceutical-drug-manufacturers.com/articles/listofdrug-related-celebritydeaths.html>.