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Banned Drugs: Long-Term Health Effects In Human

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ABSTRACT
Drug has become an integral part in human's life. The use of these drugs is regularly causing harmful effects on human's health. To protect consumer's health, Pharmacovigilance is used to ensure safety of medicines. Drugs are withdrawn from the market mainly due to observed adverse drug reaction. Damaged to liver, irregular functioning of heart, kidney failure, cancer etc are major side effects observed which leads to banned of that particular drug. Developed countries like Europe, USA banned many drugs for this prime reason. While developing countries like India are bit slower in taking actions due to lack of awareness about ill effects of medicines on human's health. Drug regulatory body needs enforce law and take initiatives to provide information about adverse effects through drug information centre. This review is an attempt to create awareness about drugs that are no longer used due to lack of safety, those once banned but reintroduced, and those that are still used despite toxicities and doubtful efficacy and drugs surrounded by controversies.

Keywords: Banned drugs, Human health, Pharmacovigilance, Safety.

INTRODUCTION

Drugs are chemicals or compounds used to cure, halt, or prevent disease; ease symptoms; or help in the diagnosis of illnesses. It may be impossible to have world free of disease, but it is possible to prevent it to a greater extent. Presently there is abundance of medicines available to be prescribed by the doctor or to be directly taken from over the counter. But before introducing the drug in the market, drug undergoes various developmental stages. During which they are tested carefully. Initially they are tested on animals and then on human during clinical trial phase. The main aim of researchers is to produce a satisfactory product with good quality. Quality medicines are achieved by maximum therapeutic effects and minimum side effects. Even though some side effects are observed when the drug is used in general population.

Each country has its own organization to monitor the circulation of drugs. Even after market approval, the safety and efficacy of the drug is continuously examined based on information gathered via Pharmacovigilance. Pharmacovigilance is a pharmacological science relating to the detection, understanding and prevention of side effects either long-term or short-term effects [1]. To collect ADR reports throughout the nation, the national pharmacovigilance program (NPP) was established by the Ministry of Health and Family Welfare in New Delhi in 2010 [1]. When the adverse effects are severe or the risks of using the drug outweigh the

benefits, or when the drug is ineffective, the country may ban the drug or the Drug Company may itself voluntarily withdraw the drug. Some drugs may cause adverse effects only when combined with particular drugs. In such cases, only the fixed dose combination is banned and not the individual drugs [2]. Several single drugs as well as fixed dose combinations have been banned for manufacture, marketing and distribution in India.

Why a drug has to be banned?

Reasons for banning a drug are as follows [3]:

1. Unexpected problems: Some of the adverse effects of drugs are well known before it is introduced into the market. While some problems arise after introduction of drug in the market. As no single individual have the same metabolism, cause of this there are chances of having different ADR's in different individual. Some adverse effects are rare and cannot be elicited by clinical trials. Leading causes of banning drugs are severe drug-induced liver diseases. But that is very rare to the extent of 1:5,000 to 1:10,000 exposures or less, which is easily missed in clinical trials and drug is introduced in the market.
2. Excess toxicity: Drugs should be thoroughly tested for developmental effects before marketing. There are alterations in species sensitivity and manifestations of developing toxicity. Practice of pharmacokinetics is an important consideration in drug testing. For example, the safety of thalidomide in pregnant women was not established. Still this drug was used in pregnant women, causing foetal toxicity and children were born with phocomelia [4].
3. Availability of safer options: A drug with less adverse effects and greater or similar efficacy is preferred. Terfenadine introduced in 1985 was banned in 1998 due to its implications in causation of cardiac rhythm abnormalities [5]. This was because fexofenadine introduced in 1997 had similar efficacy but no such adverse effects [6].
4. Harmful interactions: Drug- drug interaction is likely to cause unexpected side effects. So, it is also important to consider this factor in the developmental stage of a drug to avoid unnecessary complications. Mibefradil and astemizole were introduced in the market with known dangerous interactions with 3-4 drugs each [7]. Consequently, they showed dangerous interactions with other drugs. Therefore, they were withdrawn due to availability of other safer alternatives.
5. Irrational use: Most commonly used drug named Nimesulide for fever is been banned by various countries cause of hepatotoxicity [8]. Bromfenac sodium (NSAID) causes many cases of liver failure as it was used for prolonged time period. It has already indicated that it should be used only for a short time as it elevates liver enzymes when used over a long period of time.
6. Failure of other risk management options: FDA educates health care professionals through letters about the risks associated with a drug. Although many at times it is negotiated and ignored [9].

Process of banning a drug

The inspection of harmful side effects of drug is done by executive committee first, then they submit the results to Drug Technical Advisory Board (DTAB). The DTAB in India is the ultimate authority on striking a ban. If any drug is found to have harmful side effects, the Government issues the ban order and all manufacturers and wholesalers are asked not to stock the particular medicine. The Drug Controller of India (DCGI) notifies all state drug authorities, pharmacists associations and manufacturers about the ban of the drug [10]. Authorities are instructed to carry out inspections. Pharmacists' licenses can be withdrawn for stocking banned drugs under Drug and Cosmetics Act [11].

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Table 01: List of drugs banned globally [1]

Drug	Category	Mode of action	Banned in year	Reason for banning	Marketed name of the drug
Gatifloxacin	Antibiotic	Inhibits the bacterial enzymes DNA gyrase and topoisomerase IV	2011	It causes high blood sugar level when taken orally or iv	Gatiflo&Tequin
Rofecoxib& Valdecoxib	NSAID	Inhibits the cyclooxygenase-2 (COX-2) enzyme	2005	Increase the risk of heart attack and stroke	Vioxx &Bextra
Phenformin	ANTI-DIABETIC	Binds to the AMP-activated protein kinase		Caused lactic acidosis and increases pH in the blood	Ciba-Geigy
Roziglitazone	ANTI-DIABETIC	It works as an insulin sensitizer, by binding to the PPAR in fat cells and making the cells more responsive to insulin	2010-2011	Fast or pounding heartbeat, changes in menstrual cycles, vision changes	Avandia

Table 02: list of banned drugs which are globally discarded but still available in India [1,10,12.13,14,15,16,17,18,19,20,21,22,23,24,25,26,27,28,29]

Sr. No.	Drug Name	Use	Reason for Ban	Banned in Countries	Brand name
1.	Analgin	Pain killer	Bone marrow depression	US, Australia, Japan, Canada, Sweden, France, Nepal and Vietnam	Novalgin
2.	Droperidol	Anti-Depressant	Irregular heartbeat	Japan	Droperol
3.	Furazolidone	Anti-Diarrhoeal	Cancer	North America, Europe and many	Furoxone, Lomofen

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				Asian countries	
4.	Nimesulide	Pain killer, fever	Liver failure	Spain, Finland, Belgium, Ireland, and United States	Nise, Nimulid
5.	Nitrofurazone	Anti-bacterial cream	Cancer	US	Furacin
6.	Phenolphthalein	Laxative	Cancer	France and Italy	Agarol
7.	Phenylpropanolamine	Cold and Cough	Stroke	Canada, Cuba, Singapore, Malaysia Brazil and Oman	D'cold, Vicks Action-500
8.	Oxyphenbutazone	NSAID	Bone marrow depression	Canada, Japan, and some European countries	Sioril
9.	Piperazine	Anti-worms	Nerve damage	Europe, Japan, the USA, and Australia	Piperazine
10.	Quiniodochlor	Anti-Diarrhoeal	Damage to sight	Japan, USA, Sweden, Norway, Denmark and New Zealand	Enteroquinol

Table 2 shows some examples of drugs, which are banned in various countries but still available in India. Many of them are sold over the counter drugs are available with changed formulation but same brand name. They are available without prescription, so the general population is not aware about the serious side effects. India has serious issues with use, availability and distribution of banned drugs. Some of the drugs are mandatorily banned by Drugs Controller General of India (DCGI) but are still available in the market [30]

Reasons for availability of banned drugs in India [31]

- Just because manufacturers want to achieve their desired profit, they don't consider about fact that such drug can have severe adverse reaction. Due to this neglection and low poverty line in India, banned drugs are easily been sale without any restrictions.
- In emergency cases when there's no availability of drug, banned drugs which have same mode of action are used
- Lack of communication between the DCGI and state drug controllers
- Patients chose to have non-compliance behaviour and for any common illness they prefer OTC (over the counter) drugs or self-prescribed drug [32]
- Prescribers and patients have lack of knowledge and are unaware about the ban of any drug
- There are no official regulatory bodies to take action regarding banned drug
- Banned drugs are easily available to common public even though they are banned by government, for example nimesulide [33]

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FUTURE PERSPECTIVE:

The communication gap between the regulatory bodies and the suppliers should be minimised to avoid selling and buying of banned drugs. Banned drugs information should be widely transferred throughout country. Strict amendments should be practised by Government for safety of human health.

CONCLUSION

Long term use of such medicines can put negative impact on human health therefore ban is needed to protect the public's health and the quality of health care. The healthcare professional including physicians, nurses, pharmacist and others including the patient are all responsible to report all ADRs to the regulatory authority who can take action as soon as possible, and drugs which are banned worldwide may be not available in India too. Careful premarketing screening may also reduce the problem. Awareness programs should be conducted by the Government. The government needs to hold more public information campaigns and community activism to educate the public on the potential dangers of drug use. The government needs to make sure that the laws made by the regulatory bodies should be enforced and should punish those who distribute such drugs. Drugs banned elsewhere need to be seriously looked at and banned from use or in certain cases restricted to be used only for severe illness, in absence of other available drugs for the same indication. The CDSCO has to made a strict guidelines for our developing country India over the list of drugs have been banned by European union and USA which are developed countries. Consequently, government should implement strict laws on drug manufacturers, wholesalers and retailers.

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