APTI ijper

Regulatory Status of Banned Drugs in India

Jessy Shaji and Shital Lodha*

Prin. K M Kundnani College Of Pharmacy,

23, Jote Joy Building, Rambhau Salgaokar Marg, Colaba Mumbai - 400 005

* *For Correspondence: shitallodha@hotmail.com*

Abstract

All the formulations are meant for prevention or treatment of ailments and diseases, out of which only a few drugs are lifesaving and essential; rest of the drugs are substitutes for each other. When serious problems occur in health care there is always a "knee-jerk" response by many to impose a ban and thus provide an immediate and definitive response to the issue. While such responses may be emotionally satisfying they often represent answers which are "smarter than we are" and may end up causing more harm than good.

Banned drugs are still available in developing countries like India due to lack of law enforcement and physician awareness. Some of these drugs namely Nimesulide, Rofecoxib, Phenyl propanamine and other Over The Counter (OTC) preparations are banned by the US FDA due to their side effects such as agranulocytosis, kidney and liver failure etc, but are still being marketed in India. The government needs to enforce laws and provide information to physicians and patients regarding these drugs through drug information centers. The pharmacist should hold public information campaigns and educate consumers, and thus play an important role on eliminating the market for banned drugs.

Key words: Banned drugs, regulatory bodies, unapproved drug, .

INTRODUCTION

"PILL FOR EVERY ILL" is a saying which is being focused and pursued. It may not be possible to have a disease free world but we can aspire for solutions to relieve misery and make patient's life more comfortable to a greater extent. The main aim is to ensure good quality of life to patients. This can only be achieved with quality drugs with maximum therapeutic benefit and minimum side effects, available to all at low cost. A patient relies on his physician and prescriber for his treatment. Thus it is the duty of the physician to meet the patient's requirements to their satisfaction. A drug is usually prescribed to a patient for its positive effect but may give rise to several adverse effects. Some of the common ones that are easily available and used frequently without doctor's prescription are Phenyl propanolamine, analgin, cisapride and nimesulide [1, 2] among several others which, continue to be sold as OTC in India[3]. Coxibs were the widely prescribed drugs until the recent setback with rofecoxib, which was withdrawn from the market by the innovator due to increased risk of heart attacks and strokes observed with its long-term use[4, 5]. Analgin was widely used, easily available, relatively cheap and efficacious analgesic. Initially this drug was banned in 1974 because of the myelotoxicity but significant methodological flaws in the study led to criticism and the drug was unbanned in 1995 but as a prescription drug only. Further studies led to more controversies regarding its association with agranulocytosis and it was again withdrawn from the market in 1999.[6] It was estimated that the fatal agranulocytosis occurred in one out of 10,000 users of the drug analgin. Other serious toxic effects like life threatening exfoliative dermatitis, toxic epidermal necrolysis and renal papillary necrosis causing death in 17 to 93% cases[7].

These are used as pain-killers but latest research shows that long term use of such medicines can affect human health in various ways by damaging liver, causing irregular heartbeats, depression, and blood pressure fluctuations etc[8]. This is the prime reason that most of European countries have disqualified and banned the manufacturing and consumption of these drugs.

Numerous studies have shown life threatening ADRs with nimesulide such as hepatotoxicity, renal toxicity

Indian Journal of Pharmaceutical Education and Research
Received on 20/06/2008; Modified on 02/10/2008
Accepted on 18/11/2009

severe skin reactions, GI toxicity, and coronary artery insufficiency[9]. Pediatric nimesulide was withdrawn from the Indian market because of the potential hazards of the drug.[10, 11, 12]. Therefore the manufacturing, sale, distribution and marketing of these drugs need to be outlawed, such drugs are termed as banned drugs. More than 60,000 branded formulations are available in India.

One of the latest threats facing the global pharmaceutical industry and healthcare is the presence of spurious/substandard drugs in the market. This definition of counterfeit includes not only completely fake drugs but also those that have been tampered with, adulterated, diluted, repackaged, or relabeled so as to misrepresent the dosage, origin, or expiration date, as well as those substandard drugs that are cheaply produced in order to make unlawful profits.

A survey conducted in the states of Maharashtra and Uttar Pradesh by a government agency revealed some interesting facts: (1) according to about 70% of patients, pharmacists/chemists suggest substitute pharmaceuticals in case a prescribed pharmaceutical is not available; (2) around 78% of patients opined that chemists/pharmacists do not inform patients about such substitutions; (3) 43% of doctors accept that there are incidents of spurious/substandard drugs being sold in the market; (4) generic drugs from different manufacturers are available with differences of as much as 500% in prices; (5) inadequate quality checking by the respective drug authorities, poor drug awareness, and low literacy rates are the reasons being attributed for the flourishing market in spurious/ substandard drugs[13].

Phenyl propanolamine is associated with risk of hemorrhagic stroke, still it is the most commonly used banned drug for common cold and cough. It is a common constituent of many formulations in India[14, 15].

It is shocking that so many scheduled drugs being made available so easily in India without any prescription, and the drugs which have expired too are being sold in some areas. It is clinically proved that almost all the drugs have side effects at therapeutic levels besides toxic effects. Unwanted side effects are referred to as adverse drug reactions (ADR). The safety of combination drugs has to be thoroughly evaluated and there are considerations for the drugs that are already in the market as individual or single drug entity[16]. However, the safety profile of established drugs will change when they are combined together. There was an alarming increase in irrational fixed dose combinations (FDCs) in recent years and pharmaceutical companies manufacturing these FDCs are luring physicians to prescribe by unethical means[17, 18.]

In our country, after amendment of the Drugs Act in 1982, the Government has acquired the power to prohibit manufacture and sale of certain drugs and irrational FDCs[19].

The government, subsequently, issued the first gazette notification in July 1983 banning several drugs and their FDCs after due consideration. A ban or restricted use order is being issued on a continuous basis on observing ADRs on Indian patients. The total number of essential drugs mentioned in the 14th list of essential medicines by WHO is 312, out of which only 18 are FDCs[20]. But many of the irrational combinations are popular and widely prescribed by physicians in our country. The combinations such as tetracycline and vitamin C, quinolones and nitroimidazoles and penicillins with sulfonamides are some of the examples of irrational FDCs. There have been many combinations of analgesic and anti-inflammatory preparations available in the market, particularly that of paracetamol and ibuprofen. In line with this, is there any justification for a combination of nimesulide and paracetamol? Thus far available information suggests that such a combination of nimesulide and paracetamol would be irrational[21].

Over 70 dangerous FDCs are being sold in India under more than 1,000 brand names. Legally, when two or more individually approved drugs are combined, the mixed medicine is deemed to be a 'new' product and hence requires DCGI approval. In practice, state drug controllers merrily go on licensing such combinations even though they do not have the legal powers to do so. Once one state drug controller approves a combination, it can be sold all over the country. The result: a patient in, say, Maharashtra consumes a drug that is neither approved by the DCGI nor by the Maharashtra drug controller but by a drug controller in, say, Assam! Unless state drug controllers are made to obey the law, no improvement can occur. Such dubious FDCs entail financial burden, promote the prevalence of resistant strains of bacteria and increase unwanted effects[20]. Therefore it is important for health care professionals to be aware about recent developments in banned drugs and assess the risk-benefit ratio before prescribing. Promotion of unsafe drugs in the developing world has long attracted criticism, particularly when products have

been banned or restricted in the country of manufacture.[22, 23 24].

Many drugs that have been banned in developed countries are easily available in India[25]. Pharmacists don't hesitate to sell these drugs because doctors continuously prescribe these medicines despite knowing their implication and side effects on the patient [22]. The use, misuse and abuse of drugs have shaken the foundation of both amateur and professional sports in recent years. To protect athlete's health and to avoid unfair means, International Olympic Committee (IOC) has banned certain categories of drugs such as stimulants, narcotics, steroids, diuretics, peptide hormones etc[26]. Every country needs powerful regulatory bodies that make laws regarding the drugs that are either approved or to be banned. Decision should be unbiased. But due to lack of updated knowledge, enforcement, awareness and especially corruption, the number of controversial drugs getting government consent and their market is flourishing in India[27].

A very strong regulatory authority can improve the public health and thus can improve the pharmaceutical market in the country. Table1 shows various regulatory bodies which govern the process and procedures regarding drug laws.

As soon as these drugs are banned by regulatory bodies, in developed countries it is notified immediately to all pharmacies and physicians.

In USA, FDA is entrusted with the task of approving or rejecting drugs marketed by pharmaceutical companies. FDA ensures that newly approved drugs have passed vigorous testing which includes animal testing, clinical trials of healthy and diseased individuals. Clinical research centers provide uniform data which are pooled, examined analyzed and reported with appropriate conclusions. Finally a trial report is prepared and presented in a scientific format by experts and submitted to regulatory authorities for approval. For every 5000 compounds that enter preclinical evaluation, about 5 will proceed to the clinical trial stage, and only one will gain FDA approval for marketing in the US .The FDA also verifies safety, quality, and efficacy, along with drug interactions. "THE MARKETED UNAPPROVED DRUGS" is a policy guide issued by the US FDA outlining a prioritized, risk based enforcement approach to the manufacturer in which they have to submit applications to the FDA to show that their products are safe and effective[27].

REASONS OF AVAILABILITY OF BANNED DRUGS IN INDIA ARE

* A lengthy legal procedure to ban any drug in India which is banned in developed countries gives long time to manufacturers to manufacture these banned drugs in India. Commercial interests of pharmaceutical companies, corruption, lack of transparency and accountability is the major reason for such delay in banning procedure.[28]

* Regulatory bodies lack enforcement power.

* Due to the poverty line in India these drugs are easily marketed at low costs.

* Many private practitioners and physicians are unaware about the ban.

* Non –compliance by the patient by self prescribing the drugs for common ailments and disorders. The patient has a mindset that he gets well fast with the drug he takes like Nimesulide, Rofecoxib, Phenylpropanolamine for common ailments such as cold, cough, head ache, etc and they don't know about the side effects, whether these drugs are banned or not.[29,30]

* Because of self prescription, numbers of allergic and anaphylactic reactions are occurring frequently in India. This can be prevented by public awareness programmes regarding the status, use, and side effects of self prescription.

* Non-availability of appropriate drugs and their high cost[28, 29]

* Prescribers lack of knowledge and experience.[29,30]

* In some places such as Ludhiana, the department has no provision for notifying to hospital and doctors about the status of these banned drugs except through newspaper.

* One of the reasons for the free availability of banned drugs in the market is this communication gap between the DCGI and state drug controllers. A recent case concern phenformin formulations. The product is still available in the market after its ban order issued on 1st October 2003. A serious problem confronting the medical profession today is the lack of updating of their knowledge about existing and new drugs.

* Drug Inspectors cannot reach out & inspect every pharmacist/wholesaler because Drug Inspectors are too few.

The list of drugs prohibited for manufacture and sale

through gazette notifications is given under section 26A of drugs and cosmetics act 1940 by the Ministry of Health and Family Welfare. Till date, the Indian government has banned several FDCs and imposed restrictions on many drugs and their combinations with other drugs for its manufacturing and marketing in India. (see Table 2)

The safety of a patient during drug therapy is a vital aspect of treatment. So it is imperative for all health care professional to acquaint themselves with the list of banned drugs given in table no. 2. Further it is also imperative for the industrial pharmacists and marketing professionals to keep themselves abreast with the list of banned drugs, drugs for restricted use and banned FDCs. This ultimately helps them in formulating the right product mix and implements a proper marketing strategy[20].

PROCESS OF BANNING

When a serious problem occurs in health care there is always a "knee-jerk" response by many to impose a ban and thus provide an immediate and definitive response to the issue. While such responses may be emotionally satisfying they often represent answers which are "smarter than we are" and may end up causing more harm than good.

The classic example of drug banning has been the saga of thalidomide. Thalidomide, developed in Germany in the mid-1950's, became popular on a world-wide basis as a tranquilizer and sleep inducing medication. Thalidomide initially appeared to be safe. The fact was that it was a teratogen (capable of birth defects) associated with maldevelopment of fetal extremities. Incidentally, there is no common regulation available till date forcing banning of drugs simultaneously in all countries.

The Drug Technical Advisory Board (DTAB) in India is the final authority on imposing a ban. An executive committee examines the harmful effects of the drugs and reports the results to the DTAB. 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 DCGI notifies all state drug authorities, pharmacists associations and manufacturers about the ban of the drug. Authorities are instructed to carry out inspections. Licenses of pharmacists stocking banned drugs can be revoked under the Drug and Cosmetics Act[30]

Process of banning is given in fig. 1

Officials at the Drug Controller of India (DCGI) office, however, had a different take on the issue of banned drugs. "Screening of irrational or harmful drugs is an ongoing exercise and over 79 categories of formulations have been banned so far. With a view to ensuring proper dispensing and rational use of drugs, packing has been standardized. Even after a drug gets market approval, safety and efficacy is continuously examined on the basis of information received through pharmaco-vigilance, post-marketing surveillance and information received from other countries.

India's contribution to the world wide collection of data on the side effects of different drugs is dismal. Countries like Ireland, Switzerland and Italy with a population of about 4 million, 33million and 57 million respectively, had submitted 25, 33, and 225 adverse drug reactions on Nimesulide. Inspite of world wide ban drugs such as "Nimesulide, Phenyl propanolamine, Analgin," etc are being sold in India[27]. When a very profitable drug is banned abroad for its adverse effects, interest groups in India resist similar action here.

List of Drugs Banned by the Government of India under Section 26A of the Drugs & Cosmetics Act 1940 are given in table no.3, and are available from: http://www.cdsco.nic.in/html/Drugsbanned.html

In India, DCGI has approved the ban of 138 drugs in 2005 as compared to 39 drugs in 2003 [31]. The status of these banned drugs in India is indicated in table 4:

Fig. 2. Indicates the survey done in few pharmacies and it was found that amongst the banned drugs Phenylpropanamine is the most rapidly selling drug (54%) followed by Analgin (23%) and Nimesulide (13%) and the least being Rofecoxib (10%) which pharmacists have stopped prescribing and its marketing has almost stopped.

Fig. 3. Indicates survey was done regarding the awareness of banned drugs amongst laymen, pharmacists, students, and doctors .It was found out that 75% of laymen, 40% of the doctors and pharmacists, and 60% of science students were not aware of ban.

SUGGESTIONS

There are various suggestions, which when taken into consideration can play an important role in reducing the marketing of banned drugs in INDIA.

* All new molecules and products have to be approved by the Drugs Controller General, India (DCGI). Once a new molecule is licensed, the state drug

controllers take over and monitor pharmaceutical manufacturing facilities located in their own jurisdictions.

* Government should amend the law periodically with the consent of regulatory bodies of other developed countries. The list of banned drugs should be clearly justified to the target professionals such as pharmacist, physician, manufacturer, etc[32].

* Promotion of unsafe drugs in the developing world has long attracted criticism, particularly when products have been banned or restricted in the country of manufacture. Pharmaceutical adverts, labeling, and package inserts in developing countries often show the twin problems of exaggerated indications and minimized adverse effects. Government should look after critical issues such as drug promotion, labeling regulation of the OTC drugs, marketing of irrational FDC and banned drugs, etc[33]. Unfortunately we have not yet learned that the banning of therapeutic agents/ drugs is not warranted. The banning of the non-steroidal anti-inflammatory drug Rofecoxib is a more recent example of this. Warranting is clear identification of the known risk and communication of this fact to patient, so that they provide accurate information allowing true informed consent, such informed consents are more safe than banning. This safeguard is, however, only meaningful when there are health care consumers placed in the driver's seat who have the motivation and means to seek out these truths and are also capable of effectively using this information.

* There should be an involvement of all categories of health care professionals in ADRs and pharmacovigilance planning[34]. ADR reporting should be made mandatory as they are in developed countries. Pharmacovigilance should be more effective[35]. The aims of such programs are to contribute to the regulatory assessment of benefit, harm, effectiveness, and risk of medicines[16]. They encourage safe rational and effective use of drugs and improve public health. Further they promote understanding, clinical training and effective communication to the public[3,36].

* More drug information centers should be opened. These centers provide current, independent, unbiased, and critically evaluated drug information that can lead to enhanced quality of patient care, and improved patient outcome. Information provided by such centers helps Prescribers to choose the most appropriate drugs for the patient. They provide ward round participation, provision of drug information, adverse drug reaction monitoring, patient counseling [28,29].

* Moreover, regulatory authorities, healthcare professionals, researchers and pharmaceutical companies should join hands together to formulate guidelines for the FDC's to drive away fear from the minds of patients. The pharmacist should educate the masses on how and when to use drugs and provide information to the Prescribers and other health care professionals. It is essential for health care professionals to get acquainted with the list of drugs which are irrational and banned by DCGI. In addition, they should keep themselves updated with the notifications issued by the DCGI to curb irrational fixed dose combinations. This shall help them to use proper medicines and save patients from unsafe drugs[37].

* Reducing the number of branded drugs facilitates pharmaceutical regulation makes it easier for health care officials to educate consumers about the proper use of available medications in generic form[27,38].

* 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.

CONCLUSION

In conclusion one can say that, though several drugs are banned or restricted for sale in the developed countries such as USA these banned drugs are still being sold in developing countries such as India. Therefore it becomes important for the government to implement laws, strict on manufacturers, wholesalers and retailers'. There should be creation of awareness amongst physicians, health professionals and general public about the ADR of these drugs. If all these steps are taken in a well defined and unified way the market for these banned drugs can be eliminated permanently and rapidly.

Table No. 1. Regulatory bodies

Short Forms	Regulatory Bodies	Countries
FDA	Food And Drug Administration	United States
EMEA	European Medicines Agency	European Union
TGA	Therapeutics Goods And Administration	Australia
DCGI	Drug Controller General Of India	India
SIDC	State Institute For Drug Control	Czech Republic
NAM	National Agency For Medicines	Finland
BfArM	Federal Institute For Drugs And Medical Devices	Germany
PCHRD	Philippine Council For Health Research And Development	Philippines
SIDC	State Institute For Drug Control	Slovak Republic
MPA	Medical Products Agency	Sweden

Table No. 2. Detailed information of the banned drugs.

Generic	Name Use	Reason for ban
Analgin	Pain-killer	Bone-marrow depression
Cisapride	Acidity, constipation	Irregular heart beat
Droperidol	Anti-depressant	Irregular heart beat
Furazolidone	Anti-diarrhoeal	Cancer
Nimesulide	Pain-killer, fever	Liver failure
Nitrofurazone	Antibacterial Cream	Cancer
Phenolphtalein	Laxative	Cancer
Phenylpropanamine	Cold and Cough	Stroke
Oxyphenbutazone	NSAID	Bone marrow depressions
Piperazine	Anti-worms	Nerve damage
Quiniodochlor	Anti-diarrhoeal	Damage to sight
Practolol	Cardiac arrhythmias	Destruction of lacrimal glands
Methaqualone	Sedative, CNS depressant	Renal insufficiency, coma, death
Fenfluramine	Antiobesity	Cardio-toxicity

Fig. 1. Flow chart of process of banning:

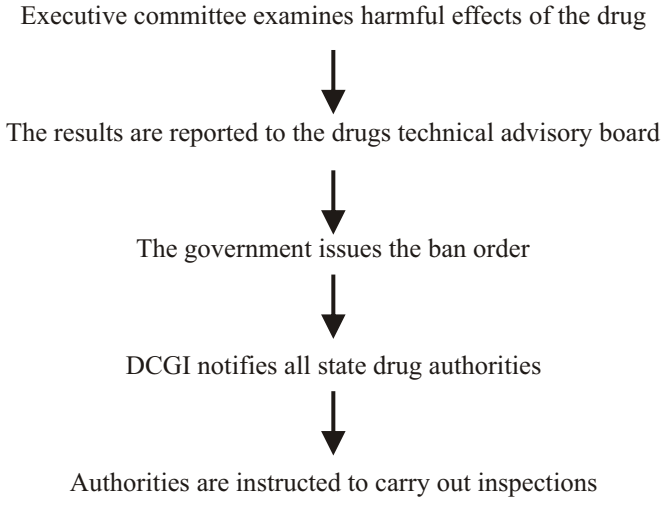


Table No. 3 Drugs prohibited for manufacture, sale and distribution from subsequent date

No.	Drugs Formulation	Effective date	Notification
1	Cosmetics Licensed as toothpaste/tooth powder containing tobacco	With immediate effect	GSR 444(E) dt.30.4.92
2	Parenteal Preparations fixed dose combination of streptomycin with Pencillin	Jan 1, 1998	GSR 93(E) dt.25.2.97
3	Fixed dose combination of Vitamin B1, Vitamin B6 and Vitamin B12 for human use	Jan 1, 2001	GSR702(E) dt.14.10.9
4	Fixed dose combination of haemoglobin in any form (natural or synthetic).	Sep 1, 2000	GSR 814(E) dt.16.12.99
5	Fixed dose combination of Pancreatin or Pancrelipase containing amylase, protease and lipase with any other enzyme.	Sep 1, 2000	GSR 814(E) dt.16.12.99
6	Fixed dose combination of Nitrofurantoin and trimethoprim.	Jan 1, 2002	GSR 170(E) dt.12.3.01
7	Fixed dose combination of Phenobarbitone with any anti-asthmatic drugs	Jan 1, 2002	GRS 170(E) dt.12.3.01
8	Fixed dose combination of Phenobarbitone with Hyoscin and /or Hyosymine	Jan 1, 2002	GSR 170(E) dt.12.3.01
9	Fixed dose combination of Phenobarbitone with Ergotmine and /or Belladona.	Jan 1, 2002	GSR 170(E) dt.12.3.01
10	Fixed dose combination of Haloperidol with any anti-cholinergic agent including Propantheline Bromide.	Jan 1, 2002	GSR 170(E) dt.12.3.01
11	Fixed dose combination of Nalidixic Acid with any anti-amoebic including Metronidazole.	Jan 1, 2002	GSR 170(E) dt.12.3.01
12	Fixed dose combination of Loperamide Hydrochloride with Furazolidone	Jan 1, 2002	GSR 170(E) dt.12.3.01
13	Fixed dose combination of Cyproheptadine with Lysine or Peptone.	Jan 1, 2003	GSR 170(E) dt.12.3.01
14	Astemizole	Apr.1, 2003	GSR191(E) dt.5.3.03
15	Terfinadine	Apr.1, 2003	GSR 191(E) dt.5.3.03
16	Fenformin	Oct.1, 2003	GSR 780(E) dt.1.10.03
17	Rafecoxib	Dec 13, 2004	GSR 810(E) dt. 13.12.04
18	Valdecoxib and it's formulation	July 25, 2005	GSR 510(E) dt. 25.07.05

Table No. 4. Status of the banned drugs in India

Banned drugs	Date of banning	Status/ availability in India
Nitrofuran	Jan 1 , 2002	Restricted sale
Cisapride	July ,2000	Banned
Astemizole	Apr 1 ,2003	Banned
Terfinadine	Apr 1 ,2003	Banned
Phenformin	Oct 1 ,2003	Available
Rofecoxib	Dec 13 ,2004	Available
Fenfluramine	Aug 14,1998	Banned
Nimesulide	2000	Available
Phenyl propanamine	Nov ,2000	Available

Fig. 2. Rapidly selling banned drugs in India.

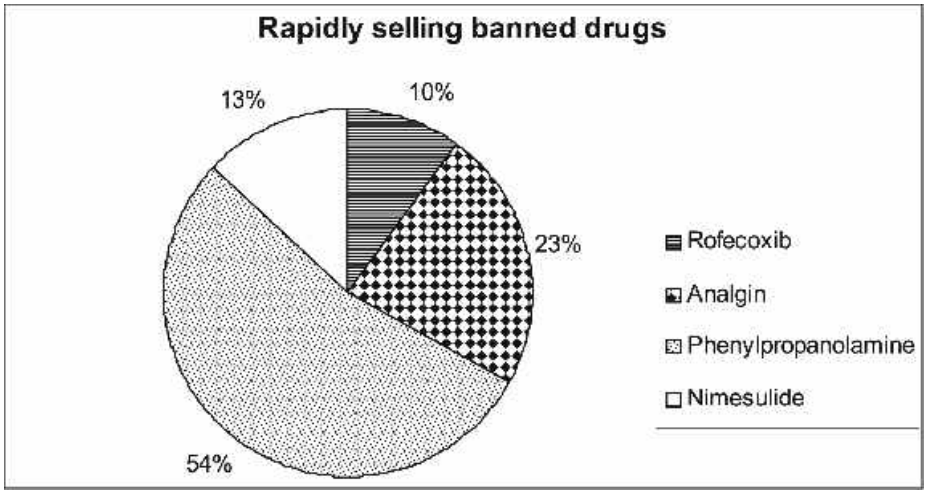
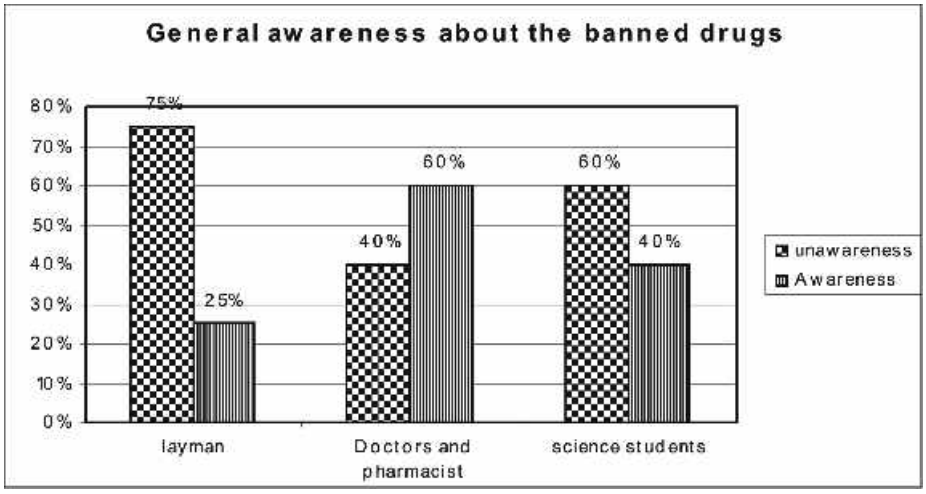


Fig. 3. General awareness about the banned drugs



REFERENCES:

1. Thawani .V, Sontakke. S, Gherpure .K, Pimpalkhute. Nimesulide the current controversy. Indian J. Pharmacol 2003; 35:121-2.
2. Panacea patient's nimesulide composition. Express Pharma, 2006; 21:129.
3. Thawani V, Sharma S, Gharpure K. Pharmacovigilance: Is it possible if bannable medicines are available over the counter? Indian J Pharmacol 2005;37:191
4. Kulkarni SK, Jain NK. Coxibs: The new super aspirins or unsafe pain killers? Indian J Pharmacol 2005;37:86-9
5. Nandave MD, Ojha SK, Arya DS. Should selective Cox-2 inhibitors be used more? Indian J Pharm Sci 2006; 68:281-5.
6. Oricha BS, Muhammad BY. Dipyrone (Novalgin, Metamizole): Banned and Unbanned: The dilemma of commonly prescribed and over the counter analgesic. Annals of African Medicine 2003; 2(2):101-2.
7. Bapna JS, Dandiya PC. Analgin: 'Its Present Status and 'Possible Hazards. Ind. J. Pharmacol 1977; 9(3):233-5.
8. Study raises doubt on painkillers safety. Express Pharma 2006; 2(3):159.
9. Rahman SZ, Khan RA. Is nimesulide safe in a cardiovascular-compromised patient? Indian J. Pharmacol 2004; 36(4):252-3.
10. Khan S. Nimesulide and adverse drug reactions: Time for a database. J Postgrad Med 2008; 54:242.
11. Kumar S. Drug linked to child death is still available in India. BMJ 2003; 326:70.
12. Saha, K. Use of nimesulide in Indian children must be stopped. BMJ.2003; 326:713.
13. Khan AY, Ghilzai NM. Counterfeit and substandard quality of drugs: The need for an effective and stringent regulatory control in India and other developing countries. Indian J Pharmacol. 2007; 39:206-7
14. Karnan WN, Viscoli CM, Brass LM et.al. Phenyl propanolamine and risk of hemorrhagic stroke. N. Engl. J. Med 2000; 343:1826-32.
15. SoRelle R. FDA warns of stroke risk associated with phenylpropanolamine, cold remedies and drugs removed from store shelves. Circulation 2000; 102:E9041-3.
16. Health ministry to double ADR monitoring centers in the country. Chronicle Pharmabiz 2006; 6(49):1.
17. Sreedhar D., Subramanian G., Udupa N., Combination drugs: Are they rational? Current Science 2006; 91(4).
18. Prakash S. Irrational combinations: No consideration for patient safety. Indian J. Pharmacol 2007; 39(5): 217.
19. Gupta R N, Irrational Combinations and Banned Drugs, August-2003, Available from URL http://www.pharmabiz.com/article/detnews.asp?Arch=a&articleid=17397&sectionid=46
20. Office of Combination Products, Food and Drug Administration, USA: available from: URL: http://www.fda.gov/oc/combination/21 CFR Part 3.2(e).
21. Kulkarni SK, Jain NK. Is there a rationale for nimesulideand paracetamol combination? Indian J Pharmacol 1999; 31:444-5.
22. Kanji N, Hardon A, Harnmeijer JW, Mamdani M, Walt G. Drugs policy in developing countries. London: Zed Books, 1992.
23. Silverman M, Lydecker M, Lee PR. Bad medicine: the prescription drug industry in the Third World. Stanford: Stanford University Press, 1992.
24. Menkes David B. Hazardous drugs in developing countries: The market may be healthier than the people, BMJ 1997; 315:1557-8.
25. Mohanty Deepakkumar, Drugs banned: yet available in India [online] 2007 [cited 2007 Jul 25] http://www.newstrackindia.com/newsdetails/533
26. Alka Beotra. Doping in sports: A perspective. Indian J. Pharmacol 1995; 27:83-8.
27. Francis P.A. Marketing unapproved drugs. Pharmabiz [online] 2006 [cited2006 Oct 11], available from: URL: http:// www.pharmabiz.com
28. Lakshmi.P.K. Is there medicine management by the pharmacist. Pharmabiz 2003; 77.
29. Tiwary P., Rajshree. Role of medicine information in promoting rational drug use, Pharma Times. 2006; 38(7):20.
30. Drug and Cosmetics Act. Available from: URL: http://www.drugscontrol.org/ban_drugs.htm
31. Drugs banned in India available from: URL: http://www.cdsco.nic.in/html/Drugsbanned.html.
32. Parmar DM, Jadav SP. Should banned drugs be mentioned clearly? Indian J. pharmacy 2006; 38(6):438.
33. Banning all drug promotion is the best option pending major reforms. J. Bioethical Inquiry 2005; 2(2):75-81.
34. Yadav S. Status of adverse drug reaction monitoring and pharmacovigilance in selected countries. Indian J. Pharmacol 2008; 40(1):S4-S9.
35. Gautam CS, Aditya S. Irrational drug combinations: need to sensitize under graduate. Indian J Pharmacol 2006; 38(3):169-70.
36. Prakash S. Pharmacovigilance in India. Indian J Pharmacol 2007; 39:123
37. Chetley A. Problem drugs. London: Zed Books, 1995.
38. Mudur G. India admits to unapproved drug formulations in market. BMJ 2003; 326:1286.