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# INTERNATIONAL JOURNAL OF CURRENT RESEARCH IN CHEMISTRY AND PHARMACEUTICAL SCIENCES

(p-ISSN: 2348-5213; e-ISSN: 2348-5221)  
www.ijrcps.com

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## Review Article

### A REVIEW ON SOME OF THE BANNED DRUGS WHICH ARE STILL AVAILABLE IN INDIA

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#### Abstract

There are a broad category of drugs used for several disorders (diabetes, cancer, arthritis etc). A number of drugs that are banned in abroad are freely available in the Indian market. The most pitiable feature is that use of these drugs is regularly causing long term implication for our physical health. Some of the common ones that are easily available and people use frequently without doctor's prescription are cisapride, pioglitazone, sibutramine, phenylpropanolamine, tegaserod, gatifloxacin, rofecoxib, rosiglitazone, nimesulide and analgin. Analgin, nimesulide, rofecoxib are non steroidal anti-inflammatory and analgesic drugs which on long term use can affect human health in various ways by damaging liver, causing irregular heartbeats, depression, blood pressure fluctuations etc. This is the prime reason that most of European countries have disqualified and banned the manufacturing and consumption of these drugs. It has been recently pointed out that Indian drug regulatory authorities have refused to ban sale of 10 drug, including gatifloxacin, rosiglitazone, rofecoxib, apart from over 80 drug combinations that are prohibited in other countries IPA have made various regulations and guidelines for the control of these drug, but still they are in use because of lack of awareness in people. So by this review we try to create awareness among people regarding the banned drugs and there reason for ban

**Keywords:** Cisapride, Pioglitazone, sibutramine, phenylpropanolamine, tegaserod.

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#### Introduction

A drug is any substance that when absorbed into the body of a living organism alters normal body function. In legal terms, a drug is 'a chemical substance used in the treatment, cure, prevention, or diagnosis of disease or used to otherwise enhance physical or mental well-being.'

Drugs undergo rigorous testing before they are introduced into the market. The efficacy as well as safety profiles of the drug are tested. In spite of this, some adverse effects of drugs appear only after the drug is used in the general population. These adverse effects are detected though a process of regular monitoring after the drug is introduced into the market and this monitoring is called pharmacovigilance<sup>1</sup>.

#### Reason for Banning a Drug<sup>2</sup>

Adverse drug reactions are the prime reasons for banning a drug. ADRs, are officially described as 'A

response to a drug which is noxious and unintended, and which occurs at doses normally used for the prophylaxis, diagnosis or therapy of disease, or for the modification of physiological function'.

Drug Controller General of India is the highest authority in India to extend the approval of any drug or to ban a drug. 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.

#### Reason for Sale and Purchase of Banned Drug in India

Cost is a key issue for consumers of medicines in underdeveloped and developing countries. In many developing countries, medicines can account for up to 90% of household expenditure on health, making the

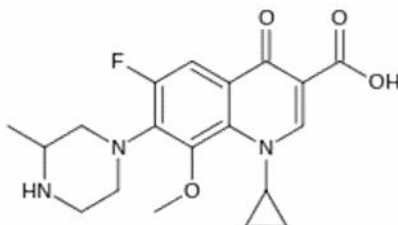
cost of medicine a key determinant in whether or not people have access. In 2005, the Indian National Commission on Macro-economics and Health labeled 10 out of 25 top selling brands of medicines in the country as being either 'irrational or non- essential or hazardous.' Those brands are listed in the table below and include a number of market leaders<sup>3</sup>.

- 4) Analgin
- 5) Cisapride
- 6) Nimesulide
- 7) Phenylpropanolamine
- 8) Pioglitazone
- 9) Sibutramine
- 10) Tegaserod

Some of the banned drugs and their reason for ban are discussed below:

- 1) Gatifloxacin
- 2) Rosiglitazone
- 3) Rofecoxib

### 1. GATIFLOXACIN<sup>4</sup> Chemical structure:



Brand names: GATIFLO, TEQUIN, ZYMA.

#### Mechanism of Action:

Gatifloxacin is an antibiotic of the fourth-generation fluoroquinolone family. It inhibits the bacterial enzymes DNA gyrase and topoisomerase IV.

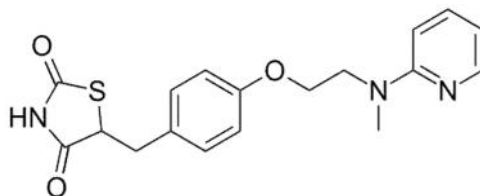
#### Uses:

Gatifloxacin is used to treat a variety of bacterial infections. It is not useful for viral infections (e.g., common cold, flu). Unnecessary use or overuse of any antibiotic can lead to its decreased effectiveness.

#### Ban of the drug

The Ministry of Health and Family Welfare, Govt of India in the Gazette notification dated on 16 March 2011, has prohibited the manufacture, sale and distribution of two drugs; gatifloxacin for systemic use and Tegaserod. The prohibitory order on gatifloxacin is applicable only for its systemic use as mentioned in the Gazette notification and does not apply to any topical formulations of gatifloxacin.

### 2. ROSIGLITAZONE<sup>5</sup> Chemical structure:



Brand name: AVANDIA, BLUTAB, DH-ROSEDIA.

#### Mechanism of Action:

Rosiglitazone acts as a highly selective and potent agonist at peroxisome proliferator activated receptors (PPAR) in target tissues for insulin action such as adipose tissue, skeletal muscle, and liver. Activation of

PPAR-gamma receptors regulates the transcription of insulin-responsive genes involved in the control of glucose production, transport, and utilization. In this way, rosiglitazone enhances tissue sensitivity to insulin.

### Medical uses

Rosiglitazone was approved by the US FDA in 1999 and by the EMEA in 2000. The drug was approved for glycemic control in people with type 2 diabetes, as measured by glycosylated haemoglobin A1c (HbA1c) as a surrogate endpoint, similar to that of other oral antidiabetic drugs.

### Adverse effects

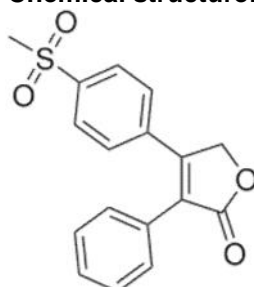
Heart failure, Heart attacks, Stroke, Bone fractures, Hypoglycemia, Weight gain, Eye damage, Hepatotoxicity.

### Ban of the drug

Rosiglitazone has the risk of heart failure and heart attacks, myocardial infarction in patients having diabetics.

European Medicines Agency on 23 September, 2010, recommended the suspension of the marketing authorizations for the Rosiglitazone — anti-diabetes medicines.

### 3. ROFECOXIB<sup>6</sup> Chemical structure:



**Brand names:** VIOXX, CEOXX, CEEOX

### Mechanism of action:

Rofecoxib selectively inhibits the cyclooxygenase-2 (COX-2) enzyme, which is important for the mediation of inflammation and pain. Unlike non-selective NSAIDs, rofecoxib does not inhibit platelet aggregation. It also has little to no affinity for COX-1.

### Adverse effects

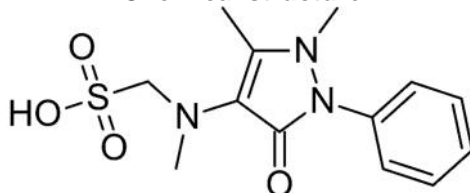
Allergic reaction (difficulty breathing; closing of your throat; swelling of your lips, tongue, or face; or

hives), abdominal pain, tenderness, or discomfort, bloody, black, or tarry stools, nausea or heartburn, blood in your vomit, a skin rash or itching, yellowing of your skin or eyes,

### Ban of the drug

On September 30, 2004, Merck withdrew rofecoxib from the market because of concerns about increased risk of heart attack and stroke associated with long-term, high-dosage use.

### 4. ANALGIN<sup>7</sup> Chemical structure:



**Brand names:** NOVALGIN, CIPLAGIN

### Mechanism of Action:

Analgin is a pyrazolone derivative with a strong analgesic, antipyretic and spasmolytic activity. Compared to the narcotic analgesics, it does not suppress the respiratory center even in high doses, has no effect on intestinal peristalsis, does not induce

constipation and does not lead to habit-forming and addiction. The mechanism of its analgesic action is associated with the inhibition of the formation of allgogenic substances, stimulation of non-opiate antinociceptive system and inhibition of prostaglandin synthesis.

### Medical uses

Novalgin (Analgin) is used in the treatment of pains of different origin and variable intensity such as toothache, headache, visceral pain or high fever. It is also prescribed for people having severe pain after operations and the pain associated with neoplastic disease or colicky pain.

### Adverse effects

- agranulocytosis / leucopenia / thrombocytopenia
- asthmatic attacks / anaphylactic shock
- urticaria / Quincke's edema
- proteinuria / interstitial nephritis / rashes

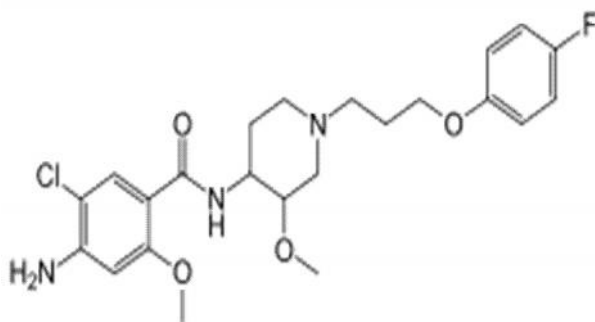
### Precautions

Novalgin (Analgin) should be used with caution in patients having known history for hypersensitivity to foods and drugs and particularly to analgesic and nonsteroidal anti-inflammatory agent, in patients suffering from bronchial asthma, Quincke's edema, chronic pulmonary infections, hypotension and unstable blood pressure.

### Ban of the drug

The Ministry of Health and Family Welfare, Govt of India in the Gazette notification dated on 18 June 2013 has banned analgin.

### 5. CISAPRIDE<sup>8</sup> Chemical structure:



**Brand Name:** PROPULSID, PREPULSID

### Mechanism of Action:

Cisapride acts through the stimulation of the serotonin 5-HT<sub>4</sub> receptors which increases acetylcholine release in the enteric nervous system (specifically the myenteric plexus). This results in increased tone and amplitude of gastric (especially antral) contractions, relaxation of the pyloric sphincter and the duodenal bulb, and increased peristalsis of the duodenum and jejunum resulting in accelerated gastric emptying and intestinal transit.

### Medical uses:

Cisapride is used in the treatment of gastro esophageal reflux (GERD) disease.

### Adverse effects

**Central & Peripheral Nervous Systems:** headache.

**Gastrointestinal System:** diarrhea, abdominal pain, nausea, constipation.

**Respiratory System:** rhinitis, sinusitis.

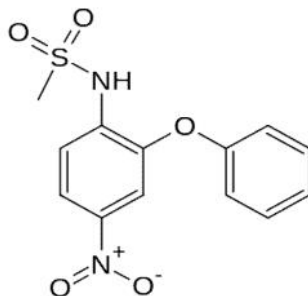
**Cardiovascular system:** tachycardia, cardiac arrhythmias, ventricular fibrillation, and QT prolongation in some cases resulting in death have been reported.

**Urinary System:** Urinary tract infection, Micturition frequency.

### Ban of the drug

The Ministry of Health and Family Welfare, Govt of India in the Gazette notification dated on 10 February 2011 has banned cisapride.

## 6. NIMESULIDE<sup>9</sup> Chemical structure



**Brand Name:** ABHINIM PH, ALSULIDE, AGRANIM.

**Mechanism of Action:** The therapeutic effects of Nimesulide are the result of its complete mode of action which targets a number of key mediators of the inflammatory process such as: COX-2 mediated prostaglandins, free radicals, proteolytic enzymes and histamine.

### Medical uses

Nimesulide is a relatively COX-2 selective, non-steroidal anti-inflammatory drug (NSAID) with analgesic and antipyretic properties. Its approved indications are the treatment of acute pain the symptomatic treatment of osteoarthritis and primary dysmenorrhoea in adolescents and adults above 12 years old.

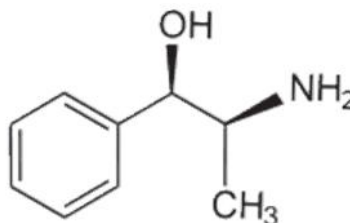
### Adverse effects

The use of nimesulide in children under the age of 12 is contraindicated. Continuous use of nimesulide (more than 15 days) can cause the following side effects: Diarrhea, Vomiting, Skin rash, Pruritis, Dizziness, Bitterness in mouth. Women should use the drug with caution during lactation and it is contraindicated during pregnancy.

### Ban of the drug

Due to concerns about the risk of hepatotoxicity, nimesulide has been withdrawn from market in many countries. The Ministry of Health and Family Welfare Govt of India in the Gazette notification dated on 10 February 2011 has banned nimesulide.

## 7. PHENYLPROPANOLAMINE<sup>10</sup>



**Brand Name:** DEXATRIM

### Mechanism of Action:

Phenylpropanolamine acts directly on alpha- and, to a lesser degree, beta-adrenergic receptors in the mucosa of the respiratory tract. Stimulation of alpha-adrenergic receptors produces vasoconstriction, reduces tissue hyperemia, edema, and nasal congestion, and increases nasal airway patency. PPA indirectly stimulates beta-receptors, producing tachycardia and a positive inotropic effect.

### Medical uses:

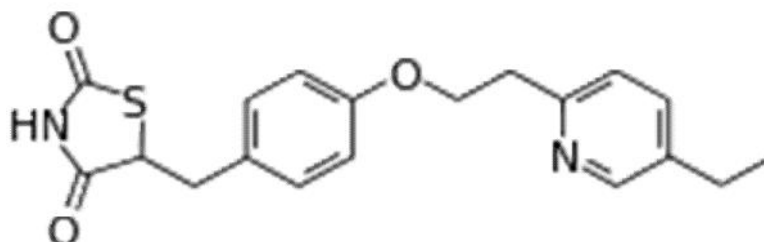
used to **dverse effects** temporarily treat cough, chest congestion, and stuffy nose symptoms caused by the common cold, flu, allergies, hay fever, or other breathing illnesses (e.g., sinusitis, bronchitis).

Some products (such as long-acting tablets/capsules) are not recommended for use in children younger than 12 years. Ask your doctor or pharmacist for more details about using your product safely

## Ban of the drug

The Ministry of Health and Family Welfare, Govt of India in the Gazette notification dated on 10 February 2011 has banned phenylpropanolamine

## 8. PIOGLITAZONE<sup>11</sup> Chemical structure



**Brand Name:** ACTOS, DUETACT

### Mechanism of action

Pioglitazone selectively stimulates the nuclear receptor peroxisome proliferator-activated receptor gamma (PPAR- $\gamma$ ) and to a lesser extent PPAR- $\alpha$ .

More recently, pioglitazone and other active TZDs have been shown to bind to the outer mitochondrial membrane protein mitoNEET with affinity comparable to that of pioglitazone for PPAR

### Medical uses

Pioglitazone is used for the treatment of diabetes mellitus type 2 either alone or in combination with a sulfonylurea, metformin, or insulin.

### Contraindication

Pioglitazone cannot be used in patients with a known hypersensitivity to pioglitazone and other thiazolidinediones.

It is ineffective and possibly harmful in diabetes mellitus type 1. It is contraindicated in diabetic ketoacidosis. Pioglitazone and all other drugs of its class (thiazolidinediones) are absolutely contraindicated in patients with heart failure. Pioglitazone is contraindicated in current bladder cancer or a history of bladder cancer.

### Adverse effects:

Hypoglycemia, liver toxicity, fractures (of arms, hand, feet), heart failure and edema, Bladder cancer, weight

gain, eye disorders (worsening diabetic macular oedema), joint pain, headache, muscle pain, back pain, erectile dysfunction, infections of respiratory tract.

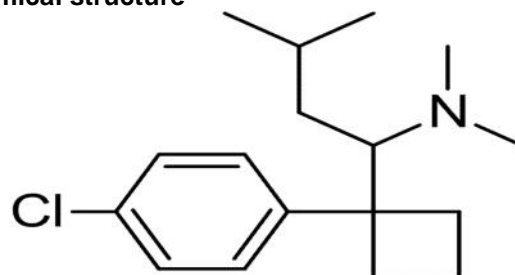
### Ban of the drug

Pioglitazone has been withdrawn in France and India.

The Ministry of Health and Family Welfare, Govt of India in the Gazette notification dated on 20 July 2013 has banned pioglitazone

## 9. SIBUTRAMINE<sup>12</sup>

### Chemical structure



**Brand Name:** MERIDIA

### Mechanism of Action:

Sibutramine produces its therapeutic effects by inhibition of norepinephrine (NE), serotonin (5-hydroxytryptamine, 5-HT), and to a lesser extent, dopamine reuptake at the neuronal synapse. By inhibiting the reuptake of these neurotransmitters, sibutramine promotes a sense of satiety and decrease in appetite, thereby reducing food intake.

### Use of sibutramine

Sibutramine is a drug used for the treatment of obesity. It affects the appetite control centre in the brain by inhibiting the reuptake of the neurotransmitters noradrenaline and serotonin.

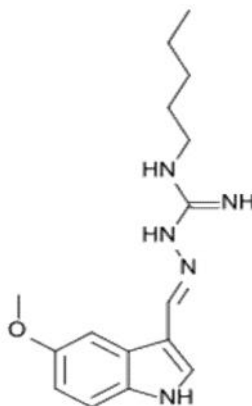
### Adverse effects

**Cardiovascular system:** sibutramine increases the risk of heart attacks and strokes in patients with a history of cardiovascular disease.

### Ban of the drug

The Ministry of Health and Family Welfare, Govt of India in the Gazette notification dated on 10 February 2011 has banned sibutramine.

### 10. TEGASEROD<sup>13</sup> Chemical structure



**Brand Name:** ZELNORM

### Mechanism of Action:

Tegaserod is a 5-HT<sub>4</sub> receptor partial agonist that binds with high affinity at human 5-HT<sub>4</sub> receptors, whereas it has no appreciable affinity for 5-HT<sub>3</sub> or dopamine receptors. It has moderate affinity for 5-HT<sub>1</sub> receptors. Tegaserod, by acting as an agonist at neuronal 5-HT<sub>4</sub> receptors, triggers the release of further neurotransmitters such as calcitonin gene-related peptide from sensory neurons. The activation of 5-HT<sub>4</sub> receptors in the gastrointestinal tract stimulates the peristaltic reflex and intestinal secretion, as well as inhibits visceral sensitivity.

Tegaserod is a selective serotonin receptor agonist. It works on the nerves of the bowel to improve bowel function. This helps you to have more normal stools.

### Medical uses:

Tegaserod is used in short term treatment of irritable bowel syndrome (IBS) in women who have constipation as their main symptom. It is also used for treating certain men and women who have a type of chronic constipation. It may also be used for other conditions as determined by your doctor.

### Adverse effects: .

Following release of tegaserod, a safety analysis showed an excess number of serious cardiovascular adverse events, including angina, heart attacks, and stroke, in patients taking tegaserod compared to patients taking placebo.

### BAN OF THE DRUG

The Ministry of Health and Family Welfare, Govt of India in the Gazette notification dated on 16 march 2011 has banned tegaserod

### Conclusion

Many of us do not know about those banned drugs use them regularly which cause long term implications in our physical health. The official first needs to lay down stringent laws and direct drug manufactures not to produce those which are banned. If doctors stop prescribing drugs that are harmful to patient's health pharmacist will stop dispensing those drugs and there will be no patients who will require these drugs.

The manufacturers can sell their products only if there are buyers (patients in need of it) so if there are no buyers manufacturer will be forced to stop manufacturing. The central drugs standard control organization will have to make stringent guidelines and look over for their implementation.

A law can be made but it's fruitful only when implemented with strict enforcement.

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