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The Negative Aspects of Nimesulide Drugs

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Abstract: *Concerns over the safety profile of mesulide, a commonly prescribed nonsteroidal anti-inflammatory medicine (NSAID), have been raised by reports of severe adverse events. Examining Nimesulide's negative effects is the goal of this review, which will focus on its hepatotoxicity, gastrointestinal risks, cardiovascular hazards, renal impairment, and dermatological responses. A careful examination of case records, clinical studies, and regulatory agency data shows a troubling trend of damage associated with mesulide.*

Results show that, especially in the Indian market, Memesulide's harmful effects are made worse by a lack of pharmacovigilance, warnings, and regulatory monitoring.

This review promotes:

1. The manufacturing and distribution of nimosulide must be immediately prohibited.

2. Improved pharmacovigilance and reporting of adverse events.

3. Encouragement of safer alternatives for NSAIDs.

The results of the study highlight how urgently regulations must be implemented to protect public health..

Keywords: Nimesulide, adverse effects, hepatotoxicity, gastrointestinal risks, cardiovascular dangers, prohibition

I. INTRODUCTION

A powerful analgesic and antipyretic, mesulide is a nonsteroidal anti-inflammatory medication (NSAID) that was first made available in the 1980s. At first, it was thought to be a secure and efficient remedy for a number of inflammatory diseases. But as time has gone on, an increasing amount of data has shown a troubling trend of negative responses linked to mesulide.

II. HISTORY

1. Early warnings: Liver damage and gastrointestinal hemorrhage linked to mesulide were first reported in the 1990s.
2. Regulatory actions: Because of worries about liver damage, the European Medicines Agency (EMA) limited the use of mesulide in children in 2002.
3. International prohibitions: Nimesulide is prohibited or subject to restrictions in a number of nations, including Canada, Australia, and the United Kingdom.

NEGATIVE IMPACT

1. Hepatotoxicity: Jaundice, liver failure, and liver damage.
2. Risks to the gastrointestinal tract: ulcers, bleeding, and perforations.
3. Cardiovascular risks include hypertension, myocardial infarction, and stroke.
4. Renal impairment: renal failure and kidney injury.
5. Dermatological reactions: toxic epidermal necrolysis, Stevens-Johnson syndrome.

INDIAN MARKET SITUATION

1. Widespread use: In spite of international concerns, mesulide is nevertheless extensively accessible in India.
2. Absence of regulation: Poor regulatory supervision and insufficient pharmacovigilance.
3. Growing reports: In India, there are more and more cases of negative responses linked to mesulide.

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JUSTIFY THE REVIEW

1. Assessing harm: Determining the frequency and intensity of side effects associated with mesulide.
2. Providing data to support regulatory action to safeguard public health is known as "informing policy."
3. Encouraging safer substitutes: Finding patients safer NSAID alternatives.

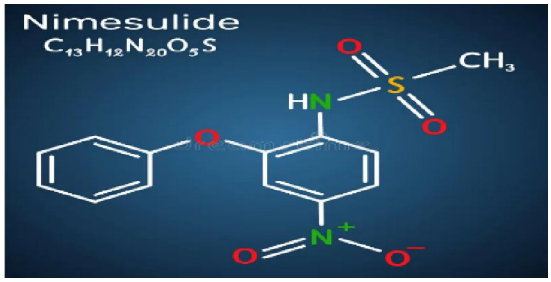
OTHER CHOICE

1. Acetaminophen
2. Ibuprofen
3. Additional NSAIDs with superior safety records

NIMOSULIDE DRUG:-

Nimesulide is a member of the sulfonamide class of nonsteroidal anti-inflammatory drugs (NSAIDs). Pain, inflammation, and fever are all frequently treated with it.

CHEMICAL STRUCTURE



ACTION MECHANISM

1. Reducing the production of prostaglandins by inhibiting the cyclooxygenase-2 (COX-2) enzyme.
2. Preventing the synthesis of molecules that cause inflammation.

APPLICATIONS

1. Inflammation and pain (such as tendonitis or arthritis).
2. A fever.
3. Dysmenorrhea, or menstrual cramps.
4. Pain following surgery.

FORMULATIONS

Nimesulide drug in Indian market available number of forms:

1. Tablets.
2. Tablets.
3. The suspensions.
4. Creams for the skin.

BRAND NAMES

Well-known Nimesulide brand names are:

1. India's Nise.
2. Europe's Mesulid.
3. Asia's Aulin.

HISTORY

The first mesulide was created in the 1960s, and its usage was authorized in the 1980s.

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DISPUTE :-

Despite its efficacy, mesulide's safety profile has raised questions, especially in relation to:

1. Liver poisoning.
2. Bleeding in the stomach.
3. Risks to the heart.

STATUS OF REGULATIONS

The regulatory status of mesulide differs across the world:

1. Prohibited in a number of nations, including the UK and Australia.
2. Limited usage in other regions (like Europe).
3. Generally accessible in India.

CRUCIAL POINTS Prior to using Nimesulide, think about:

1. Health history (e.g., blood problems, liver illness).
2. Drug interactions with other drugs.
3. Possible adverse consequences.

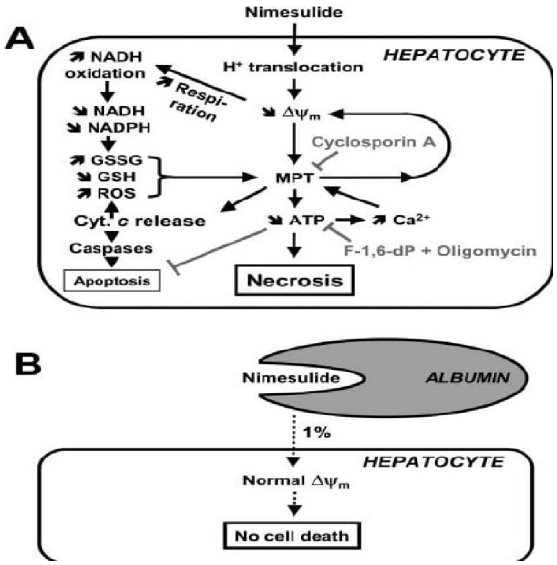
OBJECTIVES

1. To understand the principle of flame photometry and its application in ion concentration measurement.
2. To calibrate the flame photometer using standard potassium solutions.
3. To measure the potassium ion concentration in the given sample.

MATERIALS

1. Flame photometer
2. Standard potassium solutions (10, 20, 30, 40 and 50 ppm)
3. Sample solution (unknown potassium concentration)
4. Distilled water
5. Potassium chloride (KCl)

PHARMACOLOGICAL



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PHARMACODYNAMICS :-

A nonsteroidal anti-inflammatory medication (NSAID) called mesulide has the following properties:

1. Inhibition of cyclooxygenase-2 (COX-2): Lowers prostaglandin production, which has analgesic and anti-inflammatory effects.
2. Inhibition of cyclooxygenase-1 (COX-1): Leads to adverse consequences in the gastrointestinal tract.
3. Inhibition of inflammatory mediators: Lowers the synthesis of pro-inflammatory cytokines such as interleukins and tumor necrosis factor-alpha.

PHARMACOKINETICS :-

1. Absorption: After oral administration, it is quickly absorbed.
2. Distribution: The body is widely dispersed.
3. Metabolism: CYP2C9 and CYP3A4 facilitate hepatocellular metabolism.
4. Elimination: Expelled as feces and pee.

THE NEGATIVE IMPACT OF MECHANISM:-

HEPATOTOXICITY :-

1. Mitochondrial damage: Liver cell damage results from mitochondrial malfunction brought on by mesulide.
2. Oxidative stress: Liver damage is a result of elevated reactive oxygen species.
3. Hepatocytes undergo programmed cell death, or apoptosis.

GASTROINTESTINE RISK :-

1. COX-1 inhibition: Increases the risk of gastrointestinal bleeding by lowering protective prostaglandins.
2. Mucosal damage: The stomach mucosa is directly harmed.

HEART RISK

1. Elevated blood pressure: hypertension brought on by mesulide.
2. Thrombotic events: A higher chance of stroke and myocardial infarction.

RENAL DAMAGE RISK :-

1. Vasoconstriction brought on by mesulide: decreased renal blood flow.
2. Nephrotoxicity: When renal tubules are directly damaged.

DERMATOLOGICAL RESPONSE:-

1. Toxic epidermal necrolysis and Stevens-Johnson syndrome are examples of immune-mediated hypersensitivity.

ADVERSE EFFECT ON GASTROINTESTINAL SYSTEM:-

1. Bleeding in the stomach
2. Ulcers
3. The holes
4. Feeling queasy 5. Vomiting
6. The occurrence of diarrhea
7. Pain in the abdomen

HEPATOTOXICITY :-

1. Damage to the liver
2. Jaundice
3. Failure of the liver
4. Increased liver enzyme levels
5. Necrosis of the liver

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CARDIOVASCULAR SIDE EFFECTS

1. Infarction of the heart
2. A stroke
3. High blood pressure
4. Failure of the heart
5. Heartbeats

ADVERSE EFFECT ON THE RENAL SYSTEM

1. Failure of the kidneys
2. Harm to the kidneys
3. Impaired renal function
4. Hematuria
5. A proteinuric diet

ADVERSE EFFECT ON DERMATOLOGICAL SYSTEM

1. The syndrome of Stevens-Johnson
2. Urticaria 3. Skin rash 4. Pruritus 5. Toxic epidermal necrolysis

NEGATIVE EFFECT ON NERVE SYSTEM

1. A headache
2. Lightheadedness
3. Perplexity
4. Epilepsy
5. Edema in the brain

ADVERSE HEMATOLOGICAL EFFECT

1. Anemia
2. Leukopenia
3. Thrombocytopenia
4. Anemia aplastic
5. The process of hemolysis

ADDITIONAL NEGATIVE IMPACTS

1. Depression of the respiratory system
2. Bronchospasm
3. The anaphylactic reaction
4. Angioedema
5. Elevated potassium levels

ADVERSE EFFECT RISK FACTOR:-

1. Being older than 65
2. Illness of the liver
3. Disease of the kidneys
4. Heart conditions
5. Disorders of bleeding
6. Concomitant drugs (NSAIDs, anticoagulants, etc.)

CONTRAINDICATIONS AND PRECAUTIONS

1. Patients with severe liver disease should not use this medication.

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2. Patients with severe renal problems should not use this medication.
3. Patients with bleeding issues should not use this medication.
4. Exercise caution while using in heart disease patients.
5. Regularly check on kidney and liver function

INDIAN NIMOSULIDE DRUG REGULATORY ENVIRONMENT

REGULATION'S PAST

1. 1985:Nimesulide was authorized for usage in India.
2. 2002: Because of worries about liver damage, the European Medicines Agency (EMA) limits the use of mesulide in children.
3. 2006: The Central Drugs Standard Control Organization (CDSCO) of India warns of the possible liver damage of mesulide.
4. 2011: CDSCO limits the use of mesulide in children under the age of twelve.

PRESENT REGULATORY SITUATION

1. According to the 1940 Drugs and Cosmetics Act, mesulide is a prescription-only drug.
2. The production, distribution, and sale of nemesulide are governed by CDSCO.
3. State Food and Drug Administrations (FDAs) keep an eye on the distribution and sale of mesulide.

REGULATORY DIFFICULTIES

1. Insufficient pharmacovigilance.
2. Poor post-marketing monitoring.
3. Failure to disclose adverse events.
4. A lack of public knowledge.

INDIAN ADVICE AND CAUTION

1. The caution from CDSCO in 2006: "Nimesulide may cause liver damage; monitor liver function."
2. The 2011 recommendation from the Indian Academy of Pediatrics, "Avoid Nimesulide in children below 12 years."
3. Nimesulide is cautiously placed on the 2015 National List of Essential Medicines (NLEM).

INTERVENTION BY COURT

1. 2011: The Delhi High Court orders CDSCO to reevaluate the safety of mesulide.
2. 2019: The Supreme Court directs CDSCO to keep an eye on the side effects of mesulide.

RESPONCES FROM STAKEHOLDERS

1. Indian Pharmaceutical Association (IPA): Supports more stringent laws.
2. The Indian Medical Association (IMA) encourages usage with caution.
3. Consumer advocacy groups: Call for more stringent laws and more public awareness.

RECOMMENDATIONS AND GAPS

1. Make pharmacovigilance stronger.
2. Improve the reporting of adverse events.
3. Raise general awareness.
4. Reassess the safety profile of mesulide.
5. Take into account prohibiting youngsters from using mesulide.

INTERNATIONAL REGULATION OF NIMOSULIDE SUBSTANCES

NATIONAL WITH PROHIBITION ON NIMOSULIDE

1. The United Kingdom (2007): prohibited because of liver toxicity issues

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2. Australia (2008): prohibited in children under the age of twelve
3. Canada (2009): limited usage in children less than twelve
4. EU (2010): limited use in children under the age of twelve
5. US (2011): FDA disapproved because of liver damage concerns
6. Japan (2012): limited usage in children less than twelve
7. South Africa (2013): prohibited because of possible liver toxicity
8. Brazil (2014): limited usage in youngsters less than twelve

REGULATORY MEASURES

1. European Medicines Agency (EMA): Children under the age of twelve should not take this medication (2002)
2. US FDA: Manufacturers received a warning notice (2011)
3. Health Canada: Children under 12 years old: Limited usage (2009)
4. Therapeutic Goods Administration (TGA) of Australia: Prohibited for use in children younger than 12 (2008)
5. The UK banned the Medicines and Healthcare Products Regulatory Agency (MHRA) in 2007
6. Indian Regulatory Authorities: Children under 12 years old may not use this product (2011)

INTERNATIONAL RECOMMENDATION AND CAUTION

1. World Health Organization (WHO): Alerts of the dangers of liver damage
2. ICH: Pharmacovigilance Guidelines International Conference on Harmonization
3. European Commission: Alerts about blood vessel dangers

PHARMACOVIGILANCE MEASURES

1. Adverse Event Reporting: Many nations require this type of reporting.
2. Regulatory bodies need periodic safety update reports, or PSURs.
3. Risk Management Plans: Put into action to reduce hazards

MOTIVE BEHIND REGULATORY MEASURES

1. Toxicology of the liver
2. Risks to the heart
3. Bleeding in the stomach
4. Impaired renal function
5. Reactions in the skin

INDIA'S NEED FOR A BAN

1. Growing safety concerns
2. Insufficient pharmaceutical monitoring
3. The availability of safer substitutes

Some common banned drugs available in India:

Generic name	Use	Reason for ban	Brand name(s)
1.Analgin	Pain-killer	Bone-marrow depression	Novalgin, Baralgan
2.Cisapride	Acidity, Constipation	Irregular heart beat	Ciza, Syspride
3.Droperidol	Anti-depressant	Irregular heart beat	Droperol
4.Furazolidone	Anti-diarrhoal	Cancer	Furoxone, Lomofen*
5.Nimesulide	Pain-killer, Fever	Liver failure	Nise, Nimulid
6.Nitrofurazone	Anti-bacterial crème	Cancer	Furacin, Emfurazone
7.Phenolphthalein	Laxative	Cancer	Jetomisol-P*
8.Phenylpropanolamine	Cold & Cough	Stroke	D'Cold*, Vicks Action 500*
9.Oxyphenbutazone	NSAID	Bone marrow depression	Sioril
10.Piperazine	Anti-worms	Nerve Damage	Piperazine, Helmazan*
11.Quiniodochlor	Anti-diarrhoeal	Damage to sight	Enteroquinolw

*Denotes it is a combination product.
Analgin, Furazolidone and Nitrofurazone are banned for use even in animals in the United States.
Analgin is banned even in Nepal, Vietnam and Nigeria.
(Source: MIMS India, September, 2005)

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LIMITATIONS OF NIMOSULIDE DRUG'S ADVERSE EFFECT

reaction

Name of drugs	Number of patients	Number of ADRs n (%)
Diclofenac	65	19 (73)
Paracetamol	12	2 (7)
Nimesulide	10	4 (16)
Ibuprofen	6	0 (0)
Etoricoxib	2	1 (4)
Piroxicam	5	0 (0)
Total	100	26 (100)

ADR-adverse drug reactions

LIMITATIONS OF THE STUDY

1. Small sample sizes: The statistical power of several investigations was diminished by their small sample numbers.
2. Short research periods: Because most studies were brief, they could have missed long-term impacts.
3. Variable study designs: Comparisons were difficult due to variations in study designs and techniques.
4. Limited population diversity: Generalizability was limited by studies' frequent focus on particular communities.
5. Confounding factors: Confounding variables were not taken into account in several research.

LIMITATION OF THE DATA:-

1. Underreporting: Because of a lack of surveillance, adverse occurrences may be unreported.
2. Inconsistent reporting: Adverse events are reported differently in different research.
3. Limited long-term data: It's unclear how using mesulide will affect you in the long run.
4. Animal research: There are restrictions on extrapolating findings from animal studies to people.
5. In vitro research: Research conducted in vitro could not be a true representation of human physiology.

METHODOLOGICAL RESTRICTION

1. Selection bias: Research may have chosen participants based on particular traits.
2. Information bias: Data collecting that is inaccurate or lacking.
3. Measurement bias: Unreliable instruments.
4. Analytical constraints: Restrictions on statistical analysis.

REGULATORY RESTRICTION

1. Absence of uniform regulations: variations in regulations among nations.
2. Inadequate pharmacovigilance: Inadequate adverse event monitoring.
3. Low public awareness: Insufficient public instruction about the dangers of nimosulide.

OTHER MEDICATION OPTIONS FOR NIMOSULIDES :-

Better Safety Profiles for NSAIDs

1. The selective COX-2 inhibitor celecoxib (Celebrex)
2. The preferred COX-2 inhibitor meloxicam (Mobic)
3. The conventional NSAID diclofenac (Voltaren) has better gastrointestinal safety.
4. A conventional NSAID with a decreased risk of cardiovascular disease is naproxen (Aleve).
5. Ibuprofen, a conventional NSAID with a decreased risk of gastrointestinal side effects (Advil, Motrin)

ALTERNATIVES TO NSAID'S

1. Acetaminophen, an analgesic and antipyretic found in Tylenol

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2. The opioid analgesic Tramadol (Ultram)
3. Gabapentin (Neurontin), an analgesic and anticonvulsant
4. Pregabalin (Lyrica), an analgesic and anticonvulsant
5. Anti-inflammatory corticosteroids (prednisone, for example)

NATURAL AND HERBAL SUBSTITUENTS:-

1. Turmeric (Curcuma longa), an antioxidant and anti-inflammatory
2. Ginger (Zingiber officinale): an analgesic and anti-inflammatory
3. Willow bark (Salix alba) has anti-inflammatory and analgesic properties.
4. Boswellia (Boswellia serrata): an analgesic and anti-inflammatory
5. Anti-inflammatory omega-3 fatty acids

BIOLOGICAL TREATMENT

1. Etanercept, a TNF-alpha inhibitor (Enbrel)
2. TNF-alpha inhibitor Adalimumab (Humira)
3. The TNF-alpha inhibitor infliximab (Remicade)
4. Rituximab, often known as Rituxan, is a CD20 inhibitor.
5. Abatacept (Orencia), an inhibitor of T-cell activation

THINGS TO THINK ABOUT

1. Comorbidities and medical history of the patient
2. Contraindications and drug interactions
3. Treatment duration and dosage
4. Adverse effect monitoring
5. The effectiveness and reaction of each patient

PROSPECTS FOR THE FUTURE

1. Ongoing observation of unfavorable incidents
2. Examining the safety profile of mesulide
3. Creation of safer substitutes
4. Improved pharmacovigilance protocols
5. Perform epidemiological research to evaluate the risk-benefit ratio of nimesulide.
6. Create safer substitutes for nimesulide
7. Make India's pharmacovigilance systems stronger.In conclusionThe thorough literature analysis emphasizes the serious adverse effects of nimesulide medications, highlighting the necessity of prudence and regulatory intervention.

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