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Review On "Triacin-C (Triprolidine HCL, Pseudoephedrine HCL and Codeine Phosphate) Syrup

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ABSTRACT –

Triprolidine, a combination of pseudoephedrine, is used to relieve cough, sneezing, itchy or runny nose, and nasal congestion (stuffy nose) caused by allergies or the common cold. Triprolidine is an antihistamine that works by preventing the effects of a substance called histamine, which is produced by the body. Histamine can cause itching, sneezing, runny nose, and watery eyes. Pseudoephedrine is a decongestant, which decreases nasal congestion by narrowing the blood vessels and reducing blood flow to the nasal passage, is a narcotic antitussive (cough suppressant). It acts directly on the cough centre in the brain to relieve cough. Ask your pharmacist if you have any questions about your product or its use.Cough-and-cold products have not been shown to be safe or effective in children younger than 6 years. Do not use this product to treat cold symptoms in children younger than 6 years unless specifically directed by the doctor. Some products (including some 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

Do not use this product to make a child sleepy.These products do not cure or shorten the length of the common cold and may cause serious side effects.This review article provides the information of uses, side effects, and pseudoephedrine triprolidine syrup.

Codeine, phenylephrine, and triprolidine is a combination medicine used to treat runny or stuffy nose, sneezing, itching, watery eyes, cough, and sinus congestion caused by allergies, the common cold, or the flu.This medicine will not treat a cough that is caused by smoking, asthma, or emphysema.Codeine, phenylephrine, and triprolidine may also be used for purposes not listed in this medication guide.

Key words - cough, sneezing, itchy or runny nose, and nasal congestion (stuffy nose), narcotic antitussive

Introduction -

Syrup concentrated aqueous preparations of 85% of sugar or sugar substitute with or without flavouring agents and medicinal substances. In medical terminology, medicinal syrups are nearly saturated solutions of 85% of sugar in water in which medicinal substances or drugs are dissolved. Due to the inability of some children and elderly people to swallow solid dosage forms, it is fairly common today for a pharmacist to be asked to prepare an oral liquid dosage form of a medication available in the pharmacy.[1]

Triprolidine

Antihistamines such as triprolidine hydrochloride act as antagonists of the H1 histamine receptor. Consequently, they prevent histamine from eliciting typical immediate hypersensitivity responses in the nose, eyes, lungs and skin.Animal distribution studies have shown localization of triprolidine in lung, spleen and kidney tissue. Liver microsome studies have revealed the presence of several metabolites with an oxidised product of the toluene methyl group predominating.

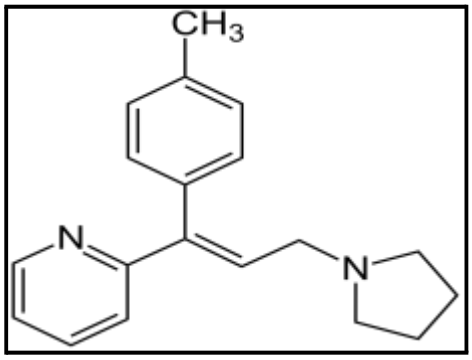

Fig - 1 triprolidine

Pseudoephedrine

Pseudoephedrine acts as an indirect sympathomimetic agent by stimulating sympathetic (adrenergic) nerve endings to release norepinephrine. Norepinephrine in turn stimulates alpha and beta receptors throughout the body. The action of pseudoephedrine hydrochloride is apparently more specific for the blood vessels of the upper respiratory tract and less specific for the blood vessels of the systemic circulation. The vasoconstriction elicited at these sites results in the shrinkage of swollen tissues in the sinuses and nasal passages.Pseudoephedrine is rapidly and almost completely absorbed from the gastrointestinal tract. Considerable variation in half-life has been observed (from about 4½ to 10 hours), which is attributed to individual differences in absorption and excretion. Excretion rates are also altered by urine pH, increasing with acidification and decreasing with alkalinization. As a result, mean half-life falls to about 4 hours at pH 5 and increases to 12 to 13 hours at pH 8.After administration of a 60 mg tablet, 87 to 96% of the pseudoephedrine is cleared from the body within 24 hours. The drug is distributed to body tissues and fluids, including foetal tissue, breast milk and the central nervous system (CNS). About 55 to 75% of an administered dose is excreted unchanged in the urine; the remainder is apparently metabolised in the liver to inactive compounds by N-demethylation, para hydroxylation and oxidative deamination.[2]

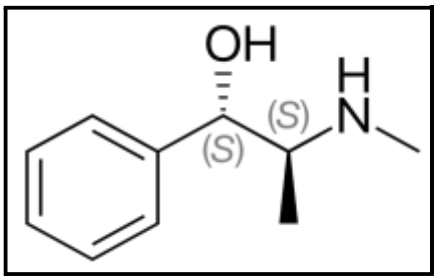

Fig - 2 Pseudoephedrine

Codeine Phosphate -

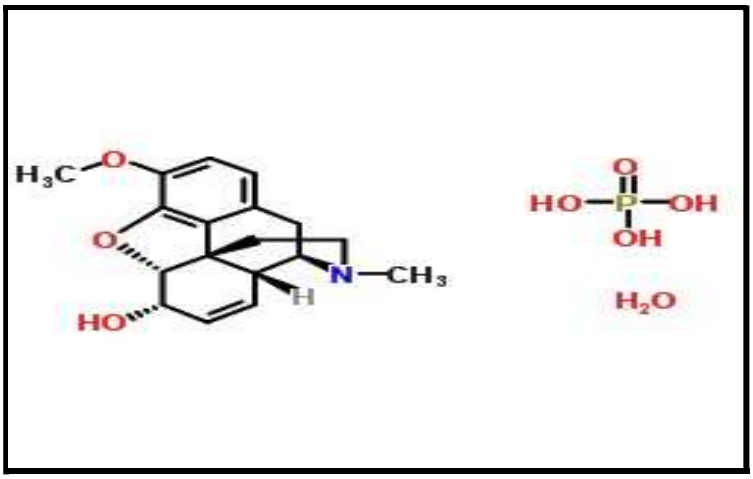

Fig - 3 Codeine Phosphate

Codeine Phosphate is the phosphate salt of codeine, a naturally occurring phenanthrene alkaloid and opioid agonist with analgesic, antidiarrheal and antitussive activities. Codeine mimics the actions of endogenous opioids by binding to the opioid receptors at many sites within the central nervous system (CNS). Stimulation of mu-subtype opioid receptors results in a decrease in the release of nociceptive. [3]

Uses -

This combination medication is used to temporarily relieve symptoms caused by the common

1. Cold, flu,
2. Allergies, or other breathing illnesses (such as sinusitis, bronchitis).
3. Antihistamines help relieve watery eyes,
4. Itchy eyes/nose/throat,
5. Runny nose, and sneezing.
6. Decongestants help to relieve stuffy nose 7) Ear congestion symptoms.[4]

Side effects -

1. Drowsiness,
2. Dizziness,
3. dry mouth/nose/throat,
4. headache,
5. upset stomach,
6. constipation, or trouble sleeping.

Formulation of syrup - TRIACIN – C

Fig - 4 formulation for syrup

TRIACIN - C

- **Brand Name**: Triacin C
- **Generic Name:** triprolidine hcl, pseudoephedrine hcl, and codeine phosphate syrup
- **Each 5 mL (one teaspoonful)-** of syrup for oral administration contains:
  1. Codeine Phosphate… 10 mg
  2. Triprolidine Hydrochloride..1.25 mg 3) Pseudoephedrine Hydrochloride..30 mg 4) Alcohol….. 4.3%.
- Inactive Ingredients
  1. sodium benzoate,
  2. methylparaben,
  3. sodium saccharin,
  4. sorbitol,
  5. glycerin,
  6. citric acid,
  7. sodium citrate,
  8. caramel flavour and
  9. USP purified water.[5]
- Manufacturer
  - Actavis Mid Atlantic LLC,
  - Alpharma USPD

- Clinical Pharmaceuticals, Inc.
- Consolidated Midland Corp.
- Harber Pharmaceutical Co.
- Moore, H.L. Drug Exchange Inc.
- STI Pharma, LLC
- Generics 12
- Triacin C consists of multiple

TRIACIN-C - CLINICAL PHARMACOLOGY -

Codeine:

Codeine probably exerts its antitussive activity by depressing the medullary (brain) cough centre, thereby raising its threshold for incoming cough impulses.Codeine is readily absorbed from the gastrointestinal tract, with a therapeutic dose reaching peak antitussive effectiveness in about 2 hours and persisting for 4 to 6 hours. Codeine is rapidly distributed from blood to body tissues and taken up preferentially by parenchymatous organs such as liver, spleen and kidney. It passes the blood brain barrier and is found in foetal tissue and breast milk.

The drug is not bound by plasma proteins nor is it accumulated in body tissues. Codeine is metabolised in the liver to morphine and norcodeine, each representing about 10 percent of the administered codeine dose. About 90 percent of the dose is excreted within 24 hours, primarily through the kidneys. Urinary excretion products are free and glucuronide-conjugated codeine (about 70%), free and conjugated norcodeine (about 10%), free and conjugated morphine (about 10%), normorphine (under 4%) and hydrocodone

(<1%). The remainder of the dose appears in the faeces.

Triprolidine:

Antihistamines such as triprolidine hydrochloride act as antagonists of the H1 histamine receptor. Consequently, they prevent histamine from eliciting typical immediate hypersensitivity responses in the nose, eyes, lungs and skin.Animal distribution studies have shown localization of triprolidine in lung, spleen and kidney tissue. Liver microsome studies have revealed the presence of several metabolites with an oxidised product of the toluene methyl group predominating.

Pseudoephedrine:

Pseudoephedrine acts as an indirect sympathomimetic agent by stimulating sympathetic (adrenergic) nerve endings to release norepinephrine. Norepinephrine in turn stimulates alpha and beta receptors throughout the body. The action of pseudoephedrine hydrochloride is apparently more specific for the blood vessels of the upper respiratory tract and less specific for the blood vessels of the systemic circulation. The vasoconstriction elicited at these sites results in the shrinkage of swollen tissues in the sinuses and nasal passages.

Pseudoephedrine is rapidly and almost completely absorbed from the gastrointestinal tract. Considerable variation in half-life has been observed (from about 4½ to 10 hours), which is attributed to individual differences in absorption and excretion. Excretion rates are also altered by urine pH, increasing with acidification and decreasing with alkalinization. As a result, mean half-life falls to about 4 hours at pH 5 and increases to 12 to 13 hours at pH 8.[6]

Precautions -

Triacin-C should be prescribed with caution for certain special-risk patients, such as the elderly or debilitated, and for those with severe impairment of renal or hepatic function. Before taking this product, tell your doctor or pharmacist if you are allergic to it; or if you have any other allergies. This product may contain inactive ingredients, which can cause allergic reactions or other problems. Talk to your pharmacist for more details.Before using this medication, tell your doctor or pharmacist your medical history, especially of: abdominal problems (e.g., chronic constipation, ileus, gallbladder disease, pancreatitis), adrenal gland problem (e.g., Addison's disease), certain brain disorders (e.g., head injury, tumour, increased intracranial pressure), breathing problems (e.g., asthma, emphysema, sleep apnea), diabetes, a certain eye problem (glaucoma), heart problems, high blood pressure, kidney problems, liver disease, mental/mood problems (e.g., depression, psychosis), seizures, stomach/intestinal problems (e.g., ulcers, blockage), thyroid problems (e.g., hyperthyroidism, hypothyroidism), urination problems (e.g., trouble urinating due to enlarged prostate, urinary retention), personal or family history of a substance use disorder (such as overuse of or addiction to drugs/alcohol), obesity.This drug may make you dizzy or drowsy or blur your vision. Alcohol or marijuana (cannabis) can make you more dizzy or drowsy. Do not drive, use machinery, or do anything that needs alertness or clear vision until you can do it safely. Avoid alcoholic beverages. Talk to your doctor if you are using marijuana (cannabis).To minimise dizziness and lightheadedness, get up slowly when rising from a sitting or lying position.This medicine may contain aspartame. If you have phenylketonuria (PKU) or any other condition that requires you to restrict your intake of aspartame (or phenylalanine), consult your doctor or

pharmacist regarding the safe use of this medicine.[7, 8]

Indications and Usages -

Triacin-C is indicated for temporary relief of coughs and upper respiratory symptoms, including nasal congestion, associated with allergy or the common cold.Triacsin C (WS 1228A), a natural intracellular long-chain acyl-CoA synthetases (ACSL) inhibitor, is from Streptomyces aureofaciens. Triacsin C inhibits TAG accumulation into lipid droplets (LD) by suppressing ACSL activity. Triacsin C is found to be highly effective against rotavirus replication [9,10]

Dosage

Dosage should be individualised according to the needs and response of the patient . Different dose quantities for children & adults.

Usual Dose:	Teas poonfuls (5 mL)
Adults and children 12 years and older	2 teaspoonfuls (10 mL) every 4 to 6 hours, not to exceed 8 teaspoonfuls (40 mL) in 24 hours.
Children 6 to under 12 years	1 teaspoonful (5 mL) every 4 to 6 hours, not to exceed 4 teaspoonfuls (20 mL) in 24 hours.
Children 2 to under 6 years	½ teaspoonful (2.5 mL) every 4 to 6 hours, not to exceed 2 teaspoonfuls

Table - 1 dose quantity of triacin c[5]

Drug/Laboratory Test Interactions with Triacin-C Syrup -

If you use other drugs or over the counter products at the same time, the effects of Triacin-C Syrup may change. This may increase your risk for side-effects or cause your drug not to work properly. Tell your doctor about all the drugs, vitamins, and herbal supplements you are using, so that your doctor can help you prevent or manage drug interactions.

Triacin-C Syrup may interact with the following drugs and products:

- Alcohol
- Alprazolam
- Amitriptyline
- Antianxiety agents
- Anticholinergics
- Antiemetics
- Antihistamines
- Antipsychotics
- Atenolol
- Carvedilol [11]

Carcinogenesis, Mutagenesis, Impairment of Fertility

No adequate studies have been conducted in animals to determine whether the components of Triacin-C have a potential for carcinogenesis, mutagenesis or impairment of fertility.

Pregnancy

Teratogenic Effects

Pregnancy Category C.

Animal reproduction studies have not been conducted with Triacin-C. It is also not known whether this product can cause foetal harm when administered to a pregnant woman or can affect reproduction capacity. This product should be given to a pregnant woman only if clearly needed.Teratology studies have been conducted with the three ingredients of Triacin-C. Pseudoephedrine studies were conducted in rats at doses up to 150 times the human dose; triprolidine was studied in rats and rabbits at doses up to 125 times the human dose, and codeine studies were conducted in rats and rabbits at doses up to 150 times the human dose. No evidence of teratogenic harm to the foetus was revealed in any of these studies. However, overt signs of toxicity were observed in the dams which received pseudoephedrine. This was reflected in reduced average weight and length and rate of skeletal ossification in their foetuses.

Triacin-C may enhance the effects of:

Monoamine oxidase (MAO) inhibitors;

other narcotic analgesics, alcohol, general anaesthetics, tranquillisers, sedative-hypnotics, surgical skeletal muscle relaxants, or other CNS depressants, by causing increased CNS depression.

This product may diminish the antihypertensive effects of guanethidine, bethanidine, methyldopa and reserpine. [5]

Side effects -

The following is a list of possible side-effects that may occur from all constituting ingredients of Triacin-C Syrup. This is not a comprehensive list. These side-effects are possible, but do not always occur. Some of the side-effects may be rare but serious. Consult your doctor if you observe any of the following side-effects, especially if they do not go away.

- Drowsiness
- Lightheadedness
- Dizziness
- Sedation
- Shortness of breath
- Nausea
- Vomiting ● Sweating
- Constipation
- Allergic reactions
- Euphoria
- Dysphoria
- Abdominal pain
- Pruritis
- Faintness
- Flushing
- Hypotension
- Palpitations
- Syncope
- Abdominal cramps
- Anorexia
- Diarrhoea
- Dry mouth
- Gastrointestinal distress
- Pancreatitis
- Anxiety
- Fatigue
- Headache
- Insomnia
- Nervousness
- Shakiness
- Somnolence
- Vertigo

- Visual disturbances
- Weakness
- Rash
- Respiratory depression
- Circulatory depression
- Respiratory arrest
- Shock
- Cardiac arrest

Overdosage

Triacin-C is composed of three pharmacologically different compounds, it is difficult to predict the exact manifestation of symptoms in a given individual. Reaction to an overdose of this product may vary from CNS depression to stimulation. A detailed description of symptoms which are likely to appear after ingestion of an excess of the individual components follows:

Overdosage with codeine can cause transient euphoria, drowsiness, dizziness, weariness, diminution of sensitivity, loss of sensation, vomiting, transient excitement in children, and occasionally in adult women, miosis progressing to non reactive pinpoint pupils, itching sometimes with skin rashes and urticaria and clammy skin with mottled cyanosis. In more severe cases, muscular relaxation with depressed or absent superficial and deep reflexes and a positive Babinski sign may appear. Marked slowing of the respiratory rate with inadequate pulmonary ventilation and consequent cyanosis may occur. Terminal signs include shock, pulmonary edema, hypostatic or aspiration pneumonia and respiratory arrest, with death occurring within 6-12 hours following ingestion.Overdoses of antihistamines may cause hallucinations, convulsions, or possibly death, especially in infants and children. Antihistamines are more likely to cause dizziness, sedation, and hypotension in elderly patients.Overdosage with triprolidine may produce reactions varying from depression to stimulation of the Central Nervous System (CNS); the latter is particularly likely in children. Atropine-like signs and symptoms (dry mouth, fixed dilated pupils, flushing, tachycardia, hallucinations, convulsions, urinary retention, cardiac arrhythmias and coma) may occur.[13]

Storage conditions -

Store at controlled room temperature 20° to 25°C (68° to 77°F)
Dispense in a tight, light-resistant container as defined in the USP.

CONCLUSION -

Triacin-C is indicated for temporary relief of coughs and upper respiratory symptoms, including nasal congestion, associated with allergy or the common cold. This combination product is used to treat symptoms caused by the common cold, flu, allergies, hay fever, or other breathing illnesses (e.g., sinusitis, bronchitis). Decongestants help relieve stuffy nose symptoms.antihistamines relieve watery eyes, itchy eyes/nose/throat, runny nose, and sneezing.Opioid cough suppressants should not be used by children younger than 18 years. Children are at higher risk for serious side effects, especially breathing problems. Talk with the doctor about the risks and benefits of this medication.Antihistamines such as triprolidine hydrochloride act as antagonists. Pseudoephedrine acts as an indirect sympathomimetic agent by stimulating sympathetic (adrenergic) nerve endings to release norepinephrine.Codeine probably exerts its antitussive activity by depressing the medullary (brain) cough centre, thereby raising its threshold for incoming cough impulses.

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