

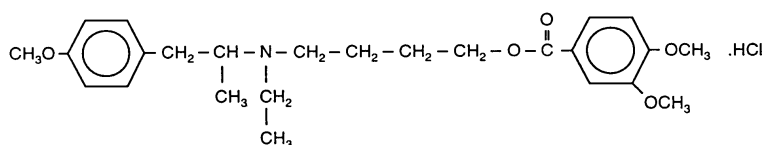
Data Sheet

Colofac[®]

Name of the Medicine

Mebeverine hydrochloride

Chemical Structure



CAS Number

3625-06-7

Description

Mebeverine hydrochloride is 4-[ethyl-[2-(4-methoxyphenyl)-1-methylethyl] aminobutyl] veratrate hydrochloride, a derivative of -phenylethylamine. It is a white to almost white, crystalline powder having a very bitter taste, very soluble in water, freely soluble in ethanol and practically insoluble in ether. The empirical formula is C₂₅H₃₅NO₅.HCl. MW: 466.0

Each Colofac tablet contains mebeverine hydrochloride 135mg. The tablets also contain acacia, carnauba wax, gelatine, lactose, magnesium stearate, povidone, potato starch, sucrose and purified talc.

Pharmacology

Pharmacodynamics

Category: Antispasmodic; smooth muscle relaxant.

Mebeverine has a direct non-specific relaxant effect on vascular, cardiac and other smooth muscle. Studies indicate that the spasmolytic activity of mebeverine is not restricted to one particular system, but the compound possesses a polyvalent spasmolytic action in which at least three types of mechanisms are involved.

- A direct musculotropic action involving Ca⁺⁺ ion exchange and stabilisation of excitable membranes;
- A competitive antimuscarinic activity of about 0.05-0.1 times that of atropine;
- A local anaesthetic activity together with potentiation of sympathetic inhibitory influences due to blockade of noradrenaline uptake into sympathetic nerve endings.

In *in vitro* studies mebeverine hydrochloride has been shown to have a papaverine-like spasmolytic effect on the smooth muscle of the ileum, uterus and the gall bladder. It possesses a strong local anaesthetic activity.

When tested *in vivo* in various species, mebeverine hydrochloride was found to be three to five times more powerful than papaverine in blocking spasm of smooth muscle and in relieving the carbachol-induced spasm of the sphincter of Oddi in rabbits, mebeverine

hydrochloride proved to be twenty times more active than papaverine. *In vivo* studies also demonstrate that mebeverine has only minor effects on normal intestinal peristalsis but possesses spasmolytic activity when hypermotility is induced. The spasmolytic activity is found in all parts of the gastrointestinal tract and in some experiments has been found to be more active on colonic smooth muscle.

Studies with mebeverine hydrochloride 100 mg tablets indicate that mebeverine is free of central anticholinergic effects, and practically free of peripheral effects with an activity of less than 0.001 times that of atropine. Mebeverine does not show central depressant or analgesic effects, and only in high doses are some central stimulating effects observed. No ganglion blocking or interference with neuromuscular transmission occurs.

Mebeverine injected intravenously in animals produces transient cardiac arrhythmias, bradycardia and ECG changes.

Pharmacokinetics

Following oral administration of ³H and ¹⁴C labelled mebeverine hydrochloride in man, absorption was followed by the appearance in the plasma of veratric acid and an oxidised metabolite of the mebeverine alcohol moiety of the drug, mebeverinic acid. The plasma half-life of these metabolites is about 2 hours.

Thus the primary metabolic step in mebeverine degradation is hydrolysis of the ester function. Maximum plasma radioactivity levels were found 1-3 hours after dosing. Binding of mebeverine to human serum albumin was 75%. The major route of excretion of the metabolites is via the urine (95%) and the peak rate of excretion usually occurs within two hours. Virtually 98% urinary recovery of the conjugated and unconjugated metabolites was observed after a period of 24 hours. No unchanged mebeverine was excreted with the urine.

Indications

Colofac tablets are indicated in the management of the irritable bowel syndrome ('irritable colon', 'spastic colon', 'functional bowel disorders', 'spastic constipation', 'nervous diarrhoea'). Colofac is used to treat the symptoms of this condition, i.e. abdominal pain and cramps, persistent, non-specific diarrhoea (with or without alternating constipation) and flatulence.

Contraindications

Hypersensitivity to mebeverine

Precautions

Although not reported, Colofac tablets should be used with caution in patients with the following conditions on the basis of potential clinical significance:

- Cardiac dysrhythmia; in particular patients with partial or complete atrioventricular heart block and/or angina or severe ischaemic heart disease.
- Hepatic dysfunction i.e. patients with advanced liver disease e.g. cirrhosis (because of metabolic pathway). Liver function tests may be indicated if patients develop gastrointestinal symptoms or jaundice suggesting hepatic sensitivity.
- Advanced renal disease (because of metabolic pathway).

Pharmaceutical Precaution - Colofac tablets contain lactose (80mg per tablet) and consideration should be given to patients with a potential diagnosis of lactose intolerance simulating irritable bowel syndrome. Patients with rare

hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

The tablets also contain sucrose and should not be used by patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency.

Use in Pregnancy

Category B2

Safe use in pregnancy has not been established with regards to possible adverse effects on foetal development. Therefore Colofac tablets are not recommended during the first trimester of pregnancy and otherwise risk-benefit must be considered in its use in pregnant women.

Teratogenicity has not been demonstrated in teratology studies in rats and rabbits.

Use in Lactation

Mebeverine is secreted in breast milk (<10 microgram/ml following an oral dose of 100mg mebeverine hydrochloride). Although problems have not been documented, as a general rule, Colofac tablets should not be given to a woman who is breastfeeding unless the anticipated benefits outweigh possible risks.

Adverse Effects

Because of the low incidence of adverse effects reported a meaningful estimate of adverse reactions is difficult to obtain.

The following side effects have been reported in clinical studies: indigestion, heartburn, dizziness, insomnia, anorexia, headache, decrease in pulse rate, constipation, general malaise

In very rare cases allergic reactions have been reported, in particular hypersensitivity, urticaria, angiodema, face oedema and exanthem.

Dosage and Administration

Adults

The recommended adult dosage is one Colofac mebeverine hydrochloride 135mg tablet three times daily, preferably 20 minutes before meals.

After a period of several weeks when the desired effect has been obtained, the dosage may be gradually reduced.

Overdosage

No data are available with regard to overdosage in humans. On theoretical grounds, it may be predicted that CNS excitability might occur in cases of overdosage.

No specific information is available on the treatment of overdosage of mebeverine hydrochloride and no specific antidote is available. Therapy with Colofac tablets should be discontinued, and the patients vital functions monitored closely. Treatment is symptomatic and supportive.

Contact the Poisons Information Centre for advice on management of overdosage.

Presentation and Storage Conditions

Colofac tablets are sugar-coated white, round, biconvex and 11mm in diameter.

Colofac tablets are available in cartons of 30 and 90 tablets in blister packs.
Store below 30°C

Further Information

Nil

Name and Address of the Sponsor

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Medicine Schedule

Prescription Medicine

Date of Preparation

06 June 2011