# HCl-Pepsin SAP

*Science-based digestive support**

Betaine (trimethylglycine) is a key human nutrient present in most tissues and is endogenously synthesized from choline in the liver and kidney. Betaine plays several important biological roles including its role as an osmoprotectant, methyl group donor, reducing plasma homocysteine levels and improving inflammation and oxidative stress.* Emerging evidence suggests its potential therapeutic application for alleviating fat accumulation in the liver and the associated liver injury.*

Hypochlorhydria is common in several medical conditions including *Helicobacter pylori* infection and prevalent in geriatric population suffering from atrophic gastritis.* Hypochlorhydria can also result due to repeated usage of acid-reducing pharmacological agents.* A hydrochloric acid (HCl) supplement such as betaine HCl is very useful in this scenario, where free HCl is produced by dissociation once it reaches the stomach.* Clinical evidence suggests that betaine HCl can be an effective therapeutic agent to temporarily lower gastric pH.* In addition, combination of betaine HCl with pepsin can synergistically help support digestion and improve malabsorption of nutrients associated with hypochlorhydria.*

## SUPPLEMENT FACTS

**Serving Size:** 1 Capsule — **Servings:** 120

| | Amount Per Serving | % Daily Value |
|---|---|---|
| Betaine hydrochloride | 700 mg | ** |
| Pepsin A (*Sus scrofa*), providing: 750,000 FCC Pepsin units | 75 mg | ** |

**Daily Value not established

**Other ingredients:** Vegetable magnesium stearate and silicon dioxide in a vegetable capsule composed of vegetable hypromellose and purified water.

**Contains no:** Gluten, soy, wheat, corn, eggs, dairy, yeast, citrus, preservatives, artificial flavour or colour, starch, or sugar.

**This product is non-GMO.**

**HCl-Pepsin SAP** contains 120 capsules per bottle.

## DIRECTIONS FOR USE

**Adults: Take 1 capsule twice daily** with meal or as directed by your healthcare practitioner. Consult a healthcare practitioner for prolonged use.

## INDICATIONS

**HCl-Pepsin SAP** can help:

- Lower gastric pH in patients with hypochlorhydria.*
- Support digestion and improve malabsorption of nutrients associated with hypochlorhydria.*
- Ameliorate fat accumulation in the liver and the associated liver injury.*

## CAUTIONS & WARNINGS

Consult a healthcare practitioner prior to use if you have a peptic ulcer or excess stomach acid; have high cholesterol; have gastrointestinal lesions/ulcers; having surgery; or if you are pregnant or breastfeeding; if you are taking anticoagulant agents or anti-inflammatory agents.
**Known adverse reaction:** Hypersensitivity (e.g. allergy) has been known to occur; in such a case, discontinue use.
**Storage Conditions:** Store in a cool, dry place, below 25 degrees celsius. Due to the sensitivity to heat and humidity of the high purity ingredients in the formula, it is ideal to store in a refrigerator. Do not use if seal is broken. Keep out of reach of children.

## PURITY, CLEANLINESS, AND STABILITY

All ingredients listed for each **HCl-Pepsin SAP** lot number have been tested by an ISO 17025 accredited third-party laboratory for identity, potency, and purity.

*** These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.**


Scientific Advisory Panel (SAP): adding nutraceutical research to achieve optimum health

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*For healthcare professional use only.*

## BETAINE HYDROCHLORIDE

Betaine (trimethylglycine or N,N,N-trimethylammonioacetate) is a key human nutrient, present in most tissues, with the highest concentrations found in kidneys and the liver. In the human blood plasma, the typical concentration of non-protein bound form of betaine ranges between 20–70 µmol/l.[1,2] Betaine is endogenously synthesized from choline in the liver and kidney.[2] Betaine plays a number of important biological roles including its role as an osmoprotectant, methyl group donor, prevention of cardiovascular diseases by reducing plasma homocysteine levels, especially in patients with homocystinuria, and improving inflammation and oxidative stress.[2-4] Recent emerging evidence supports the potential therapeutic use of betaine and the possible mechanisms by which it can attenuate liver injury.[2]

## BETAINE HCL IN HYPOCHLORHYDRIA

Hypochlorhydria occurs due to a lack (or absence) of acid in the gastric fluid. It can be a resultant of several medical conditions including *Helicobacter pylori* infection or autoimmune metaplastic atrophic gastritis.[5, 6] A study in men and women aged 60 and above showed that over 30 percent of the study population suffered from atrophic gastritis, a condition marked by suppressed or no acid secretion.[7] Another study showed that 40% of postmenopausal women have no basal gastric acid secretions.[8]

Repeated administration of acid-reducing agents, such as proton-pump inhibitors (PPIs) or $H_2$-receptor antagonists, used commonly to treat symptoms of gastroesophageal reflux disease or peptic ulcer disease can also induce hypochlorhydria.[9] Gastric acid is critical in oral drug absorption, and hypochlorhydria can cause drug-drug interactions reducing drug efficacy.[9]

A hydrochloric acid (HCl) supplement given in an encapsulated oral dosage form is very useful in this scenario, where the supplement produces free HCl by dissociation once it reaches the stomach. Betaine hydrochloride is produced as a result of the reaction between anhydrous betaine and HCl. Betaine hydrochloride is converted to betaine when it enters the alkaline environment of the small intestine.[2]

In a pilot study of 6 healthy volunteers with baseline normochlorhydria (fasting gastric pH < 4), hypochlorhydria was induced using rabeprazole until gastric pH > 4 was achieved for 15 minutes.[9] Oral supplementation of 1500 mg betaine HCl with 90 mL of water significantly lowered gastric pH after administration. Although, the re-acidification period was transient, betaine HCl was well tolerated by all participants.[9] More long-term studies with a large population is warranted. Nevertheless, it can be concluded that betaine HCl can be an effective therapeutic aid to temporarily lower gastric pH.

## OTHER PHYSIOLOGICAL BENEFITS OF BETAINE

The primary role of betaine in the kidney is cellular osmoprotection of the inner medulla which has a high and constantly variable osmolarity environment.[2, 10] Betaine is a non-perturbing osmolyte and can be accumulated to high concentrations in the cells without any harmful effects.[10] An interesting role of betaine in the liver is that it functions as a methyl donor in one-carbon metabolism. This critical role of betaine has stimulated research interest in the therapeutic supplementation of betaine for liver injury management.[11] Betaine is required in the cytoplasm for the remethylation of homocysteine to methionine.[11] Methionine is a precursor to the universal methyl donor in the body, adenosylmethionine (SAM).

Fat accumulation in liver cells is a common feature of many liver diseases. Fatty liver (hepatic steatosis) is prevalent in the obese and in those with excessive alcohol intake.

Researchers investigated what effect supplementation with betaine would have in rats fed a high-fat diet. Endpoint measures included regulation of one-carbon metabolism as well as liver lipid accumulation induced by a high-fat diet in rats.[12] Rats were supplemented with one of three diets: a liquid diet (35% fat) (control), a high-fat diet (71% fat), or a high-fat diet plus betaine (1% g/L).[12] After three weeks, rats in the high-fat-diet group had increased total liver fat concentration, liver triglycerides, liver TBARS, and plasma TNF-α.[12] The high-fat diet also decreased adenosylmethionine concentration, the S-adenosylmethionine concentration, and the S-adenosylmethionine/S-adenosylhomocysteine ratio compared to the control, and it altered the expression of genes involved in one-carbon metabolism.[12] The group receiving betaine had a substantially increased hepatic S-adenosylmethionine concentration (about fourfold) and exhibited a reduction in fatty liver or hepatic injury.[12] Moreover, in the betaine-supplemented group, there was a normalization of the gene expression of BHMT, GNMT, and mgAT, which code for important enzymes of one carbon metabolism related to liver fat accumulation.[12] Authors concluded that the regulation of the gene expression of mgAT by betaine supplementation provides a novel mechanism by which betaine supplementation regulates lipid metabolism and prevents accumulation of fat in the liver.[12]

## ROLE OF PEPSIN

The endopeptidase proteolytic enzyme pepsin secreted in the stomach, contributes to the partial hydrolysis of proteins into peptides in the stomach.[13] Similar to other protease enzymes, pepsin is produced from an inactive proenzyme precursor, pepsinogen, stored in stomach's chief cells and released by exocytosis.[13]

High-dose PPI therapy can have a serious long-lasting effect on gastric acid secretion.[13] In the absence of an acidic environment, pepsinogen cannot be converted to active pepsin.[14] In animal models, the use of PPI has been shown to lower pepsinogen secretion.[15, 16] However, in humans, the same has not been thoroughly studied. It is known that the presence of *H. pylori* increases the effect of PPI, which can affect the gastric reacidification therapy.[13]

The synergistic supplementation of pepsin along with betaine HCl may help support digestion and improve malabsorption of nutrients associated with hypochlorhydria.

## REFERENCES

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