

Use and Efficacy of the Lipid adsorbent formoline L112 in Overweight and Obesity Therapy

1. Preliminary remarks

1.1 Product safety

formoline L112 is a registered class III medical device; it has been registered as a lipid adsorbent for the entire EU under number DE/CA66/Certmedica/001. The quality and effectiveness of the active ingredients are strictly controlled prior to manufacture. The claimed effects of the product were evaluated by several independent experts as authorized by a state agency and its performance has been officially confirmed within the EU certification process.

1.2 Composition

The main ingredient of **formoline L112** consists of natural, indigestible fibres (β-1,4 polymer of D-glucosamine and N-acetyl-D-glucosamine) in specification L112. Additional ingredients are: cellulose, vitamin C, tartaric acid, silicon dioxide and magnesium stearate (of vegetable origin).

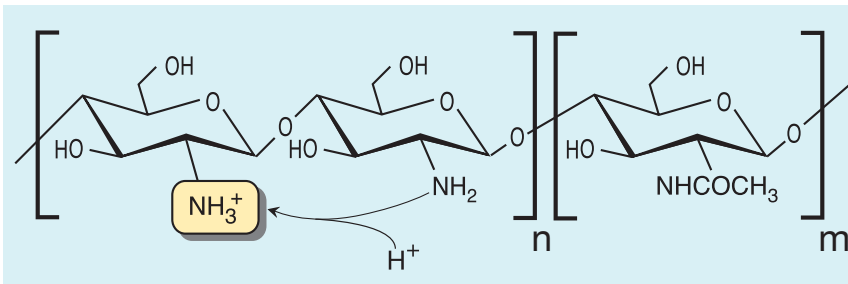


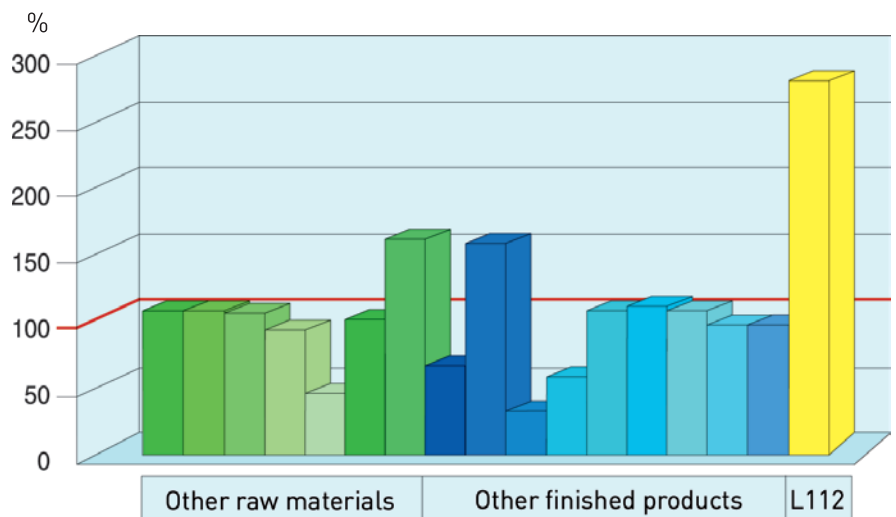
Figure 1: Polyglucosamine consisting of n parts D-glucosamine and m parts N-acetyl-D-glucosamine.

formoline L112 does not contain any flavour enhancers, preservatives or colours and is free of gelatine, gluten, lactose, and cholesterol. L112 is also suitable for diabetics, since a bread unit calculation is not necessary.

1.3 Active ingredient

The active ingredient polyglucosamine in L112 is known to be a lipid adsorbent that is active in the gastrointestinal tract (Fig. 1). Decisive for the fat binding capacity of **formoline L112** is the optimal quality of the raw material. Independent studies have shown that the fat adsorption capacity of the raw material in **formoline L112** is superior to that of other polyglucosamine preparations (Fig. 2). This capacity was about three times the average of comparison preparations and thus facilitates a correspondingly lower dose of the active agent. [1]

Figure 2: Fat binding capacity of L112 in comparison with other natural fibre preparations (red line = average value = 100%) [1].



1.4 Indications

Lipid adsorbent to

- Help reduce excess weight
- Help long-term weight control
- Help lower cholesterol intake from diet

1.5 Recommendation for use

- For weight reduction: take 2 tablets, twice daily **formoline L112** with 2 main meals with highest fat content.
- For weight maintenance 1 tablet, twice daily should suffice.

Take **formoline L112** with sufficient liquid (at least 250 ml of water), to ensure the best possible uptake and transport of tablets through stomach.

We recommend that you drink sufficient quantity of water (at least 2-3 litres) daily, as **formoline L112** is a dietary fibre.

The body requires adequate nutrients, including fat-soluble vitamins such as A, D, E and K, and essential fatty acids. To meet these requirements, you should only take **formoline L112** with 2/3 main meals daily. Along with this, we recommend at least one

meal containing beneficial oils and fats to provide your body with the fat-soluble vitamins and essential fatty acids. Multivitamin supplements may also be required.

For optimum weight loss, combine **formoline L112** with a balanced diet (with reduced calorie intake and fat content).

Information for Experts

1.6 Contraindications

- During pregnancy and breast-feeding, weight loss should not be initiated or initiated under close medical supervision. Adequate supply of fats is essential for embryonic development, and for ideal care of the infant with mother's milk.
- Should be given to growing children and teenagers only after medical consultation.
- Not suitable for infants and children (up to the age of three).
- In case of chronic digestive problems (e.g. constipation, after intestinal surgery), metabolic disorders or intake medication which reduces the constipation, **formoline L112** should only be taken after medical consultation.
- Do not take fat-soluble medicines (including the contraceptive pills) or vitamins within 4 hours of taking **formoline L112**.
- Do not take **formoline L112** if you are prone to allergies or allergic to crustaceans or any of the other ingredients.
- Do not take **formoline L112** if you are underweight (BMI < 18.5).
- Anyone over the age of 80 years should lose weight only on the advice of doctor.

1.7 Effect limitations

formoline L112 can effectively support weight loss in overweight and obesity. However, without a long-term change in behaviour only moderate weight loss is possible. **formoline L112** can optimally act as a lipid adsorbent only if the food ingested contains relevant quantities of fat.

If food that does not contain any fat or an extremely low-fat meal is ingested together with **formoline L112**, then **formoline L112** cannot act effectively. Other components of diet like for e.g. sugar, carbohydrates, protein, alcohol are not bound by **formoline L112** and will be metabolized normally.

1.8 Recommended applications

With **formoline L112** it is possible to bind a majority of the nutritional fats in the gastrointestinal tract. To lose weight specialist organizations recommend a low-fat diet that contains no more than 40 g fat each day. However, switching to a low-fat diet is very difficult for many people. **formoline L112** already with a diet containing 60 - 80 g fat per day facilitates successful weight loss. **formoline L112** mainly affects weight loss caused by high-fat food such as fatty meat, sausages, butter, and crisps, nuts and ice-cream.

During the first few days of taking **formoline L112**, it is possible for transient constipation - caused by an increased ingestion of fibre - to develop as part of the adaptational processes in the

intestinal tract. Adequate hydration of at least 2 - 3 litres daily should definitely be observed. Especially suitable are non-caloric beverages such as mineral water, fruit tea, herbal tea, etc.

2. Action mechanisms of polyglucosamine (L112)

Polyglucosamine (L112) acts locally in the digestive tract in many different ways; The individual mechanisms of action complement one another synergistically in the treatment of obesity and the metabolic syndrome.

2.1 Lipid adsorption - the primary mechanism of efficacy

All natural fibres (biopolymers) also possess lipid-binding properties to a slight degree. However, it has been confirmed that polyglucosamine fibres possess the ability to adsorb or bind therapeutically relevant quantities of fat.

1 g L112 binds more than 700 g oil.

The enormous fat binding capacity of polyglucosamine (L112) was confirmed in an assay designed to mirror the relationships

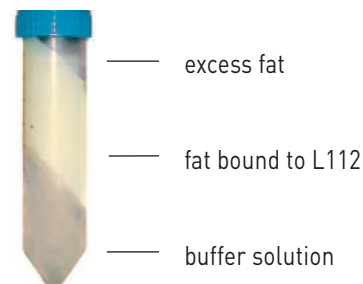


Figure 3: The high fat binding capacity of L112 can be seen in the broad fraction of fat (middle phase) bound to **formoline L112**. Raisch et al., 2005 [2].

in the digestive tract [2]. In this regard the lipid binding capacity of **formoline L112** was tested with olive oil (lipid phase) and corn starch served as the comparison substance. The quantitative analysis determined that 1 g polyglucosamine (L112) could bind 718 g nutritional fat in vitro (Figure 3).

After taking L112, the active ingredient polyglucosamine (L112) which comes into contact with gastric acid is protonated in the stomach. In this condition polyglucosamine (L112) with its very high affinity is enabled to bind a majority of the monomeric fatty acids and the nutritional cholesterol (in the duodenum) via ionic bonds (electrostatic attraction): the positively charged amino groups (NH₃⁺) of the glucosamine residues (cations) bind the negatively charged acid residues (COO⁻) of the fatty acids and the nutritional cholesterol. This very strong attraction leads to a self-stabilizing, ordered, molecular gel structure. If L112 is taken as recommended along with a fatty meal, the resulting polyglucosamine gel can be optimally distributed.

After passage through the intestines, the lipophilic agglomerate composed of polyglucosamine (L112) with the bound lipids is

excreted in a natural manner. Fatty stools usually do not occur because of the complex binding of the lipids to the polyglucosamine gel.

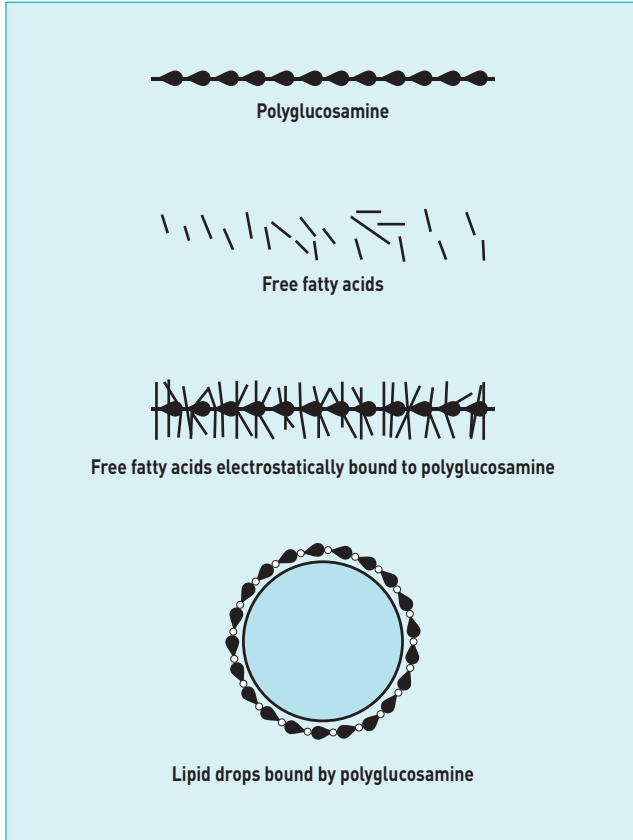


Figure 4: Lipid adsorption, modified according to Hennen W. J., 1996

The normally extremely efficient resorption of lipids that occurs through the wall of the small intestine proceeds at a notably reduced rate in the presence of polyglucosamine (L112). The mono-fatty acids (ionic bonds) required for emulsification, the non-polar lipids and the undigested fats (lipophilic interactions) are mainly bound to polyglucosamine (L112) and can no longer be resorbed.

2.2 Secondary mechanisms of efficacy

2.2.1 Saturation

The fibre and bulk materials polyglucosamine (L112) and cellulose, due to their swelling capability, also cause satiety to a limited degree.

2.2.2 Promotion of motility

If polyglucosamine (L112) is ingested as recommended with adequate fluid (e.g., 2-3 litres), the indigestible fibres - because of the swelling - increase the peristalsis of the intestinal wall and promote motility. The formation of a gel with the bound lipids increases the slipperiness of the chymus. This improves the rate of digestion and shortens the time of passage through the intestines. Polyglucosamine (L112) and the bound lipids are more rapidly excreted. Polyglucosamine (L112) when used correctly acts like a mild laxative [3].

3. Clinical studies

3.1 Weight loss

Clinical studies show that the use of polyglucosamine (L112) in combination with an unchanged diet in 2/3 (222/332) of the subjects led to a weight loss of 4.2 kg on average after 3 months [4]. In a broadly-based clinical study, Waldstein et al. confirmed that polyglucosamine (L112) reduces fat intake from the nutrients [4].

Taking L112 supported the weight loss of subjects in a randomized, placebo-controlled clinical study using calorie-reduced nutrition and significantly surpassed the results versus placebo (Fig. 5) [5].

The calorie-reduced diet resulted in an average weight loss of 2.5 kg in 4 weeks under placebo therapy. In contrast, the subjects taking polyglucosamine (L112) along with consuming a calorie-reduced diet lost 6.7 kg in the same time period [5].

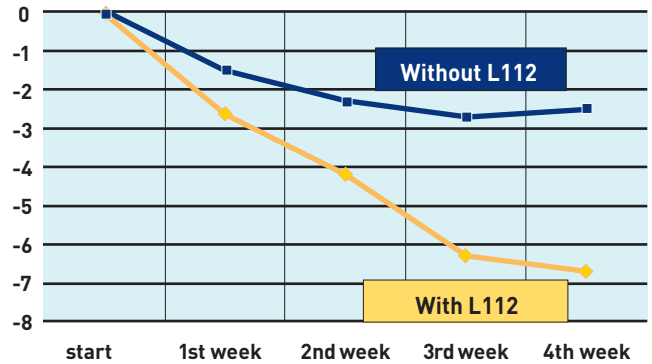


Fig.5: Cumulative weight loss/week in kg

3.2 Weight loss under L112

A current, non-interventional study (observational) confirms the efficacy of **formoline L112**. The study was conducted with 232 patients (BMI > 26, diabetes mellitus type 2). [6]

50% of the subjects also took **formoline L112** in addition to the specified change in nutrition (F-group); the remaining 50% received the nutritional course with or without placebo (standard therapy, S-group). After 12 weeks of therapy, the results were analysed.

Patients in the F-group reduced their body weight during the 12 weeks by 4.2 kg on average; those in the S-group only lost 2.8 kg. This means that the weight loss was 50% greater in the group supported by **formoline L112**. [6]

The study clearly confirms the clinical relevance of the additive benefit of **formoline L112**. This especially can be seen in the reduction of the waist measurement and thus the visceral fatty tissue. During the observation period, the waist measurement of the subjects in the F-group was reduced on average by 4.5 cm versus 3.4 cm in the S-group. This means that under addition therapy with **formoline L112** the waist measurement of the patients was reduced approximately 32% more significantly than in the comparison group. [6]

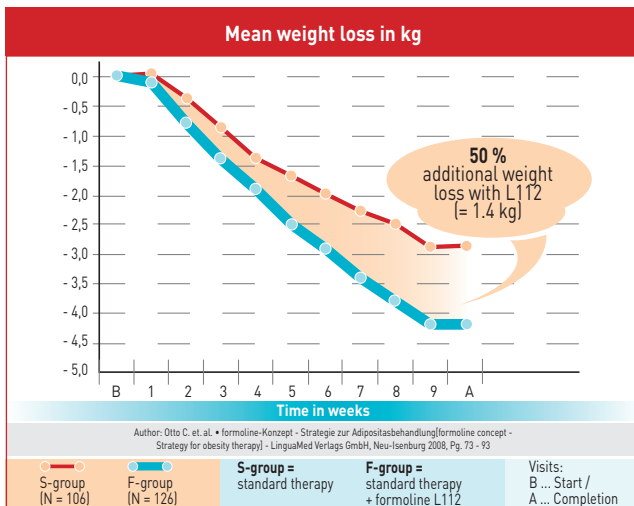


Figure 6: Weight loss under formoline L112 in comparison to standard therapy [6]

3.3 formoline L112 is generally a well-tolerated lipid adsorbent in the treatment of obesity and overweight

Taking **formoline L112** is associated with a very low probability of developing undesirable and unpleasant side effects. In extremely rare cases (less than 1/10,000 users), an adverse reaction in the form of constipation, flatulence or an allergic reaction was reported. These symptoms were temporary and disappeared rapidly without medical intervention. The cause of constipation is usually inadequate hydration while simultaneously increasing the fibre intake. **formoline L112** thus can be considered to be a very well tolerated preparation in obesity therapy. [6]

4. Discussion

In summary it can be concluded that **formoline L112** is an effective and safe product for supporting overweight therapy and weight control. L112 is very well tolerated and can be taken over the long term. [7][8]

The reduced resorption of lipids under L112 leads to a reduced intake of energy and thus contributes to weight loss. The result is an improvement in the overall state of health (e.g., the metabolic syndrome) in overweight individuals. The effect of lipid adsorption was documented for polyglucosamine and also specifically for L112. Contradictory results are unknown for polyglucosamine (L112). [6][7][8]

With **formoline L112** and a low-fat diet, it is possible to achieve notable successes. The recommendations for **formoline L112** correspond to the physiological nutritional recommendations of the specialist organisations for healthy nutrition (with 60 - 80 g fat / day). Thus, **formoline L112** assists in learning healthy and reasonable nutritional habits and in maintaining them over the long term. [8]

Lasting successes in obesity therapy require a long-term change in nutrition focusing on a low-calorie and low-fat diet combined with an adequate individualized exercise therapy and **formoline L112**. [8]

When used as an aid for losing weight, **formoline L112** can significantly increase patient compliance. Incorrect nutritional habits can only be changed in an incremental manner and thus achieve significant and long-term weight loss. [9]

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