

Dietary fibre to correct nutritional mistakes

- The main substance L112, a dietary fibre of natural origin, reduces the caloric intake from dietary fats by up to 2/3.
- scientifically proven efficacy
- excellent tolerance
- available in 2 strengths – as needed

1. Preliminary remarks

1.1 1.1. Product safety

formoline L112 is a Medical Device certified throughout the European Union. It is registered under number "DE/CA64/000381125". The efficacy and quality of the active ingredient are strictly examined prior to manufacturing.

Independent experts, authorised by a notified body, carried out evaluations of the stated intended purpose, and officially confirmed the performance of the medical device during the EC design examination.

1.2 Composition

The active ingredient of formoline L112 is an indigestible fibre of natural origin (β -1.4 polymer of D-glucosamine and N-acetyl-D-glucosamine) in the specification L112. In the following referred to as polyglucosamine L112.

formoline L112 does not contain any flavour enhancers, preservatives or colourants and is free of gelatine, gluten, lactose and cholesterol. formoline L112 is also recommended for diabetics.

1.3 Indications

Lipid adsorbent to support:

- Treatment of overweight
- Weight control
- Lower cholesterol intake from diet

2. Mechanism of action of polyglucosamine (L112)

2.1 Active ingredient

The active ingredient polyglucosamine L112 acts as a lipid adsorbent in the gastrointestinal tract. Polyglucosamine fibres have the proven ability to adsorb, bind respectively therapeutically relevant quantities of lipids.

Polyglucosamine L112 acts in multiple ways in the digestive tract; the individual mechanisms of action complement each other's activity synergistically in the management of weight loss.

2.2 Lipid adsorption – the primary mechanism of action

Polyglucosamine L112 is indigestible.

After ingesting formoline L112, the active ingredient (polyglucosamine L112) is protonated in the stomach, when it comes into contact with gastric acid. In this state, polyglucosamine L112 is able to bind to a substantial amount of fatty acids through ionic bonding (electrostatic attraction): The positively charged amino groups (NH_3^+) of the glucosamine residues (cations) bind the negatively charged acid residues (COO^-) of the fatty acids from the diet. This attraction leads to a self-stabilising molecular gel structure. This forms a highly lipophilic area, which attracts other lipophilic substances, such as cholesterol (lipophilic interaction). Ingesting the recommended dose of formoline L112 with a fatty meal allows the resulting polyglucosamine gel to have an optimal effect.

Lipid adsorption

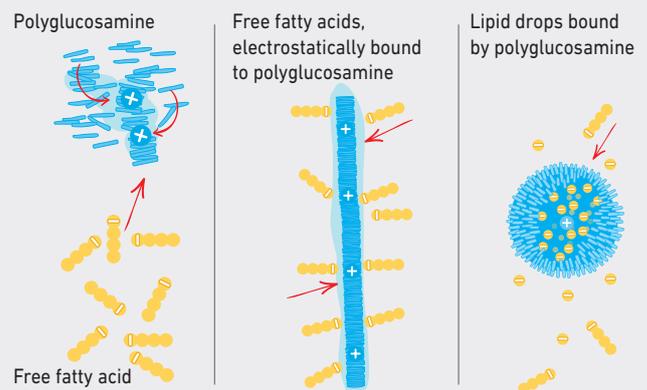


Figure 1: Lipid adsorption, modified according to Hennen W. J., 1996 [1].

The crucial factor for the high fat binding capacity of formoline L112 is the optimum quality of the raw material used. Each batch of raw material is tested and only the raw material with a fat binding capacity of at least 680 g/1 g will be accepted and released for the production of formoline L112.

The extremely efficient process of absorption of the lipids through the intestinal wall of the small intestine is considerably diminished in the presence of polyglucosamine L112. The bile acids required for emulsification as well as the mono-unsaturated, non-polar lipids and undigested fats are bound to polyglucosamine L112 and can no longer be absorbed. [2]

A placebo- controlled preclinical study confirmed that the caloric intake from dietary fat absorption was reduced by up to two thirds with polyglucosamine L112 (fig. 2). This is proof of the enormous fat binding capacity of polyglucosamine L112 in vivo as well. [3] The bound dietary fats cannot be absorbed in the small intestine. There are no fatty stools when using formoline L112. Taking formoline L112 significantly lowers caloric intake. If the intake of calories is less than the calories burned, then, as a matter of this imbalance, weight loss will occur.

Reduction of Lipid uptake from food fats

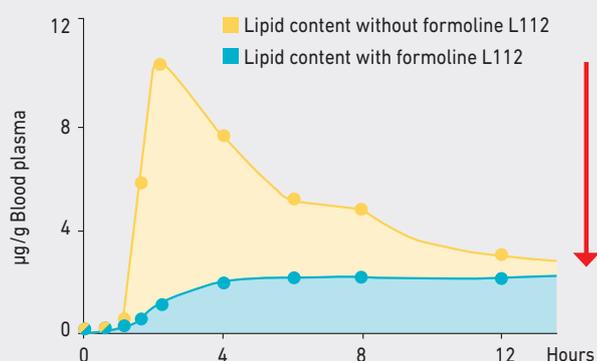


Figure 2: Lipid uptake into the blood plasma with and without polyglucosamine L112 according to Cnubben 2016 [3].

3. Directions

3.1 How to take formoline L112

formoline L112 is recommended for persons up to 75 kg, formoline L112 EXTRA containing 50% more of active ingredient for persons weighing more than 75 kg.

Both products can be swallowed whole unchewed with sufficient liquid (at least 250 ml water) for optimum effect and to ensure best possible passage of the tablets into the stomach.

■ For weight loss:

Take 2 tablets of formoline L112 or formoline L112 EXTRA twice a day with the two main meals with the highest fat content, ideally towards the end of a meal.

■ For weight maintenance:

Take 1 tablet of formoline L112 or formoline L112 EXTRA twice a day with two main meals with the highest fat content, ideally towards the end of a meal.

Due to the high fat binding capacity of formoline L112, it cannot only bind to dietary fat but also fat-soluble (lipophilic) active ingredients (e.g. steroids) or fat-soluble vitamins (A, D, E, K). It is therefore advisable to take formoline L112 at least 4 hours apart from the aforementioned products. formoline L112 may interfere with the adsorption of fat-soluble active substances.

To meet the body's requirements of fat-soluble vitamins A, D, E and K and essential fatty acids, we recommend taking formoline L112 with only two out of three main meals each day.

You should eat at least one meal containing beneficial oils and fats to provide your body with the fat-soluble vitamins and essential fatty acids it needs. Multivitamin supplements may be taken additionally.

To support weight loss with formoline L112, we recommend a healthy, well balanced fat- and calorie-conscious diet. As formoline L112 is rich in dietary fibre, we recommend that you drink at least 2 - 3 litres of fluid daily.

Low-calorie drinks, such as (mineral) water, unsweetened fruit and herbal teas, etc., are particularly suitable. In rare cases, usually in the first few days, taking formoline L112 may lead to constipation caused by an increased intake of dietary fibre.

3.2 Recommendations for use

One of the causes of overweight and obesity seems to be food high in energy density, especially in the form of dietary fats. Many overweight people consume around 100 - 140 g of fat per day. As one gram of fat contains about twice as much energy as carbohydrates or proteins, limiting the intake of fat is an effective way of losing weight. [4]

However, many people find it difficult to adjust and reduce their intake of fat accordingly. The use of formoline L112 as an effective lipid adsorbent can bind to substantial amounts of dietary fats in the gastrointestinal tract and therefore restrict energy absorption. [3]

formoline L112 is particularly suitable for people who are overweight and who cannot or do not want to follow radical low-fat diets. Thus it already supports a successful weight reduction with fat-conscious nutrition with 60 - 80 g fat per day.

3.3 Contraindications

formoline L112 should only be taken after consulting your doctor in the event of:

- Long-term medication regimens
- Serious gastro-intestinal problems (ulcerative colitis, Crohn's disease, diverticulitis, short bowel syndrome, peptic ulcer, irritable bowel syndrome, medically treated reflux, etc.) and after surgery of the gastrointestinal tract.
- Chronic digestive problems (constipation, gastrointestinal motility, etc.)
- Growing children and adolescents
- Elderly (over 80 years)
- Long-term medication regimens, particularly medications that reduce bowel movements.

formoline L112 should not be taken by the following persons:

- Infants and children up to the age of three
- Individuals who are underweight (BMI < 18.5)
- Individuals with a known allergy to crustaceans or any of the other ingredients

Pregnancy and breastfeeding

During pregnancy and breastfeeding, weight loss measures should only be initiated under close medical supervision as an optimum nutrient supply is essential for embryonic growth and development and for breast milk production, the best nourishment for an infant.

4. Clinical studies of weight loss

4.1 Double-blind placebo-controlled clinical trial in slightly overweight patients with hyperlipidaemia (Cornelli et al. 2008)

In a double-blind, placebo-controlled study, a total of 60 overweight people (BMI 26 - 30 kg/m²) received a polyglucosamine preparation or placebo in combination with appropriate physical activity. The results confirmed that taking a polyglucosamine preparation combined with additional physical activity leads to a significant decrease in body weight and has a positive impact on a pre-existing metabolic syndrome (MS). [6]

Obesity parameters after 4 months

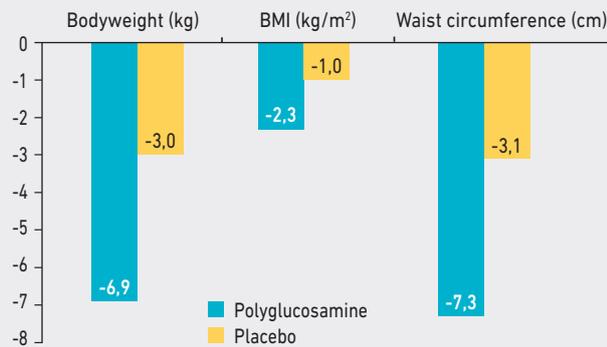


Figure 3: Significant decrease in body weight, BMI (kg/m²) and waist circumference (cm) with polyglucosamine and placebo (according to Cornelli 2008). [5]

4.2 Efficacy of polyglucosamine for weight loss – verified by a randomised, double-blind, placebo-controlled clinical trial (Pokhis et al. 2015)

A study involving 115 participants has confirmed that the consumption of formoline L112 leads to a 30 % higher weight loss versus a guideline treatment, both groups based on the standard guideline weight management with a hypocaloric diet (-500 kcal) and light physical activity. [6]

The trial participants followed a standard treatment based on a calorie-reduced diet and increased daily physical activity and took 2 x 2 tablets of formoline L112 or a placebo for at least 24 weeks.

- ▶ By taking formoline L112, participants lost 30 % more weight versus the standard guideline treatment of a calorie-conscious diet and light physical activity.
- ▶ A weight loss of 5 % of the initial weight had already been achieved by 52 % of participants in the formoline L112 group after only 8 weeks on average. In the placebo group, this was the case for only 20 % of participants

Significant advantage of weight loss

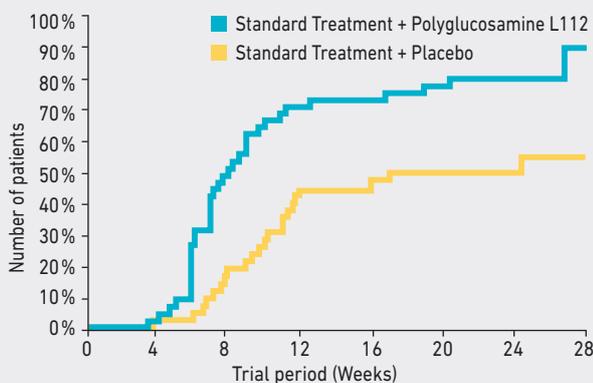


Figure 4: Estimating percentage of patients with weight loss of 5 % of initial body weight, Pokhis 2015. [6]

Thus, weight loss in the formoline L112 group was around 30 % more successful than in the placebo group. This advantage is also maintained for 3 months and 6 months after treatment.

4.3 A randomised, double-blind, placebo-controlled clinical trial of polyglucosamine in the treatment of overweight and obesity (Stoll et al. 2017)

This three-month study with 64 participants shows that polyglucosamine L112 is more effective in weight reduction than Orlistat (60 mg). In the formoline L112 group, participants lost an average of 6.7 kg, significantly more than with Orlistat (-4.8 kg, p<0.01, t-test). [7]

4.4 Randomised, double-blind, placebo-controlled clinical long-term study in the treatment of obesity (Cornelli et al. 2017)

The study with 100 participants (BMI 30 - 35 kg/m²) shows that taking 2 x 2 tablets of polyglucosamine L112 within 12 months achieved a 50 % higher weight loss than with a comparable hypocaloric diet (-10 %) and increased exercise.

- ▶ By taking polyglucosamine L112, body weight and waist circumference decreased significantly more (12.1 kg, -12.7 %; 13.3 cm, -11.6 %) than under placebo (8.0 kg, -7.8 %; 10.2 cm, -8.8 %; p < 0.001, ANOVA). (Fig. 5)

Weight loss within 12 months

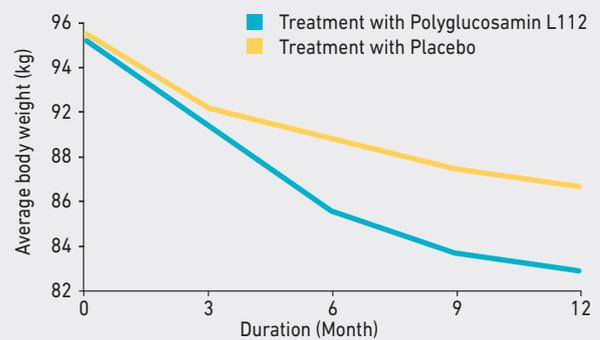


Figure 5: Change in body weight within a year [8]

- ▶ Blood pressure, plasma lipids, blood sugar and hs-CRP were reduced by a much greater amount in the polyglucosamine L112 group than in the placebo group. (Fig. 6)

Improvement of blood values

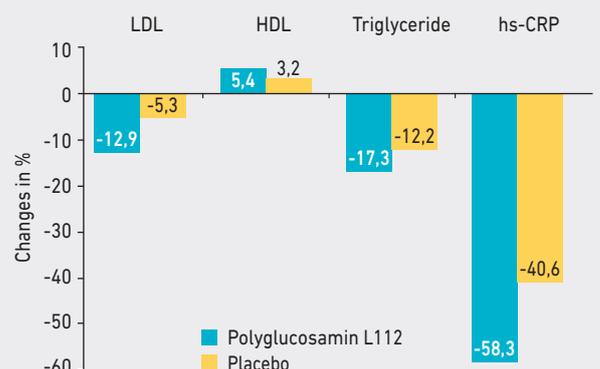


Figure 6: Change of blood values in 12 months. [8]

- ▶ The treatment was very well tolerated, with only a few cases of constipation occurring. 97 participants (49 (L112) and 48 (placebo)) completed the study. [8]

The significant reduction in LDL cholesterol (-8.67 vs. -1.0 mg/dl, p = 0.0252) was also confirmed in a randomized, placebo-controlled study on 116 patients. [9]

4.5 Tolerability

formoline L112 is generally considered as being very well tolerated. In very rare cases, undesirable effects (less than 1 in 10,000 users) such as constipation, flatulence or an allergic reaction were reported. These complaints were only temporary and soon disappeared without medical intervention. Constipation is usually induced by inadequate fluid intake accompanied by an increased consumption of dietary fibre. formoline L112 can therefore be regarded as well-tolerated for weight management.

4.6 Limitations on use

formoline L112 can effectively aid weight loss in overweight and obese patients. Another important factor for successful weight reduction is a healthy diet combined with a moderate level of daily physical activity. formoline L112 will only work effectively as a lipid adsorbent if the meal taken contains a relevant amount of fat.

formoline L112 is not suitable for people who follow a low-fat diet. Other food components, such as sugar, carbohydrates, protein or alcohol, cannot be bound by formoline L112; they will either be converted into energy or eventually be stored as body fat.

5. Discussion

In summary, it can be concluded that formoline L112 is an effective and safe product to assist weight management including weight loss and maintenance. formoline L112 is very well-tolerated and suitable for long-term use.

Decreased adsorption of lipids resulting from taking formoline L112 leads to a reduction in energy intake and therefore contributes to clinically relevant weight loss. [5-8] An improvement in the overall health status (e.g. metabolic syndrome) can be seen in overweight people. [4] The effect of lipid adsorption of polyglucosamine L112 has been documented. [3]

If taken in accordance with the recommendations mentioned in the leaflet, formoline L112 in combination with a health-conscious low-fat diet containing 60 - 80 g of fat daily is able to lead to notable weight loss in overweight people.

Long-term weight reduction requires a change in diet via a fat and caloric conscious diet, hand-in-hand with a level of physical activity which is appropriate for the respective individual.

The dietary recommendations for formoline L112 correspond to

the nutritional guidelines for a healthy diet as recommended by nutritionists with the objective of achieving sensible eating habits over the long-term.[4]

formoline L112 helps individuals to gradually learn to eat a healthy, sensible diet and to maintain this behaviour over the long-term.[6][8]

It will also enable the yo-yo effect to be counteracted. All diets that radically deplete the body of its nutrient stores over a long period of time will lower the basal metabolic rate. This can eventually result in undesirable rapid weight gain at the end of such radical dietary modifications. [10]

Used as an aid to lose weight, formoline L112 can help to achieve significant and long-term weight loss. This success will motivate and improve patient compliance.[5-8]

Bibliography:

1. Hennen W. J. (1996): Chitosan. Woodland Publishing, Pleasant Grove, USA.
2. Xia W. et al. (2011): Biological activities of chitosan and chitoooligosaccharides. *Food Hydrocolloids* 25: 170 – 179. DOI 10.1016/j.foodhyd.2010.03.003.
3. Cnubben N. H. P. et al. (2016): A single oral dose of a polyglucosamine influences the bioavailability of [9-14C]-Oleic acid in adult female Göttingen minipigs. *BMC Obesity* 3(18): 1-12. DOI 10.1186/s40608-016-0096-2.
4. Hauner H. et al.: Evidenzbasierte Leitlinie: Prävention und Therapie der Adipositas. Hrsg: Deutsche Adipositas-Gesellschaft, Deutsche Diabetes-Gesellschaft, Deutsche Gesellschaft für Ernährung, Deutsche Gesellschaft für Ernährungsmedizin, Version 2014, www.adipositas-gesellschaft.de/fileadmin/PDF/Leitlinien/S3_Adipositas_Praevention_Therapie_2014.pdf.
5. Cornelli U. et al. (2008): Use of polyglucosamine and physical activity to reduce body weight and dyslipidemia in moderately overweight subjects. *Minerva Cardioangiologica* 56(5 Suppl 1): 71 – 78.
6. Pokhis et al. (2015): Efficacy of polyglucosamine for weight loss – confirmed in a randomized double-blind, placebo-controlled clinical investigation. *BMC Obesity* 2(25). DOI 10.1186/s40608-015-0053-5.
7. Stoll M. et al. (2017): Randomized, double-blind, clinical investigation to compare orlistat 60 mg and a customized polyglucosamine, two treatment methods for the management of overweight and obesity. *BMC Obesity* 4(4): 1 – 9. DOI 10.1186/s40608-016-0130-4.
8. Cornelli U. et al. (2017): Long-term treatment of overweight and obesity with polyglucosamine (PG L112): Randomized study compared with placebo in subjects after caloric restriction. *Curr Dev Nutr* 2017;1:e000919. DOI: 10.3945/cdn.117.000919.
9. Lütjohann D. et al. (2018): Influence of chitosan treatment on surrogate serum markers of cholesterol metabolism in obese subjects. *Nutrients* 10 (72). DOI 10.3390/nu10010072.
10. Konsensus-Konferenz: Rationale Therapie mit formoline L112, Frankfurt (2009).

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formoline L112 EXTRA is recommended for people weighing more than 75 kg. It contains 50 % more of active ingredient.

Medical Device

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