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Assessment of the effect of esterified propoxylated glycerol (EPG) on the status of fat-soluble vitamins and select water-soluble nutrients following dietary administration to humans for 8 weeks

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ABSTRACT

This double-blind, randomized, controlled study assessed the effect of esterified propoxylated glycerol (EPG) on fat-soluble vitamins and select nutrients in human subjects. For 8 weeks, 139 healthy volunteers consumed a core diet providing adequate caloric and nutrient intakes. The diet included items (spread, muffins, cookies, and biscuits) providing EPG (10, 25, and 40 g/day) *vs.* margarine alone (control). EPG did not significantly affect circulating retinol, α-tocopherol, or 25-OH D_2, but circulating β-carotene and phylloquinone were lower in the EPG groups, and PIVKA-II levels were higher; 25-OH D_3 increased but to a lesser extent than the control. The effect might be related to EPG acting as a lipid "sink" during gastrointestinal transit. No effects were seen in secondary endpoint measures (physical exam, clinical pathology, serum folate, RBC folate, vitamin B_{12}, zinc, iron, calcium, phosphorus, osteocalcin, RBP, intact PTH, PT, PTT, cholesterol, HDL-C, LDL-C, triglycerides). Gastrointestinal adverse events (gas with discharge; diarrhea; oily spotting; oily evacuation; oily stool; liquid stool; soft stool) were reported more frequently by subjects receiving 25 or 40 g/day of EPG. In general, the incidence and duration of these symptoms correlated directly with EPG dietary concentration. The results suggest 10 g/day of EPG was reasonably well tolerated.

1. Introduction

Esterified propoxylated glycerols (EPGs) represent a family of fat- and oil-like substances, resembling triglycerides in structure and appearance, but modified to prevent or limit their digestion when consumed in food. They consist of multiple propylene glycol units inserted between the glycerol and fatty acid moieties of fats and oils. Their poor absorption results in a low- to no-calorie profile when substituted for fat in the diet.

The present study evaluated the possible effects of dietary EPG on the circulating levels of fat-soluble vitamins and select nutrients, along with its tolerability, when administered to healthy volunteers for 8 weeks.

2. Materials and methods

This study was sponsored by ARCO Chemical Company, Newton Square, Pennsylvania, and conducted at Chicago Center for Clinical Research, Chicago, Illinois, between January and March of 1997. The study was conducted under the principles of the World Medical Assembly Declaration of Helsinki and its amendments. The study protocol, amendments, and written informed consent were reviewed and approved by the Schulman Associates Institutional Review Board, Inc. (Cincinnati, OH), in conformance with 21 CFR 50 and 21 CFR 56. A signed informed consent statement was obtained from each subject at the first visit prior to any study procedures.

2.1. Selection of study subjects

Generally healthy male and female volunteers age 18–50 years within −10%/+30% of the ideal body weight for height, based on the Metropolitan Life Insurance Company tables, 1983 without significant abdominal disorders.

Abbreviations: EPG, esterified propoxylated glycerol; 25-OH D_2, vitamin D, ergocalciferol; 25-OH D_3, vitamin D, cholecalciferol; PIVKA II, proteins induced in vitamin K absence; RBC, red blood cell; RBP, retinol-binding protein; PTH, parathyroid hormone; PT, prothrombin time; PTT, partial thromboplastin time; HDL-C, high-density lipoproteins; LDL-C, low-density lipoproteins.

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2.2. Study design

The study, which lasted 8 weeks, was conducted using a double-blind, randomized and controlled design with four parallel groups. To maintain balance among the treatment groups, the groups were stratified by age (18–29 and 30+), sex, and estimated caloric need (1800–2400 and 2600–3000). At least 139 healthy adult male and female eligible subjects were enrolled and were randomized to one of the following treatment groups: control (ordinary triglycerides from margarine); 10 g/day EPG (EPG 10); 25 g/day EPG (EPG 25); or 40 g/day EPG (EPG 40).

For the evaluation of the response to treatment, the following outcome variables were measured at baseline and regular intervals:

- Primary Endpoints
  Serum β-carotene, retinol (vitamin A), α-tocopherol (vitamin E), 25-OH D_2 (vitamin D, ergocalciferol), 25-OH D_3 (vitamin D, cholecalciferol), phylloquinone (vitamin K_1), and PIVKA-II (proteins induced in vitamin K absence).
- Secondary Endpoints
  Changes from baseline in serum folate, RBC (red blood cell) folate, vitamin B_{12}, zinc, iron, calcium, phosphorus, osteocalcin, RBP (retinol-binding protein), intact PTH (parathyroid hormone), PT (prothrombin time), PTT (partial thromboplastin time), cholesterol, HDL-C (high-density lipoproteins), LDL-C (low-density lipoproteins), and triglycerides.
  Changes from baseline in urine concentrations of zinc, sodium, potassium, creatinine, calcium, and phosphorus.
  Secondary endpoints also included tolerability and nutrient intake [% calories from fat (saturated, monounsaturated, polyunsaturated), carbohydrate, and protein; α-tocopherol; calcium; cholesterol; dietary fiber; energy; folacin; insoluble and water-soluble dietary fiber; iron; phosphorus; potassium; total protein; selenium; total carbohydrate; total fat (saturated, monounsaturated, polyunsaturated); vitamin A; vitamin B_{12}; vitamin D; and zinc].
  Tolerability was assessed by the incidence of 14 specific gastrointestinal adverse events: passing gas; gas with discharge; abdominal bloat/cramp; heartburn; diarrhea; constipation; urgency of bowel movement; fecal incontinence; oily spotting; oily evacuation; oily stool; liquid stool; soft stool; and hard stool.

2.3. Test material

The version of EPG tested in this study was EPG-05 HR/ST 45:55 [lot numbers 850308 and 900445]. EPG was incorporated into spreads, muffins, cookies and biscuits, prepared and coded so that neither the subject nor the staff member administering the food was aware of its composition.

2.4. Treatment

From Days 1 through 56, study subjects received study meals that incorporated two biscuits and two pats of spread (margarine or EPG) at breakfast; one muffin, one cookie, and one pat of spread at lunch; and one biscuit, two cookies, and one pat of spread at dinner. These items were intended to provide a total of 0 (control), 10, 25, or 40 g of EPG daily, divided approximately equally among the study meals (breakfast, lunch, and dinner on weekdays; brunch and dinner on weekends). In an effort to maintain a stable body weight for each subject, supplemental snacks were also provided, as needed, as a source of additional calories. Drinks such as diet/low-sodium soft drinks, regular, sparkling, and flavored water were provided for consumption off-site; water was consumed *ad libitum*.

A "core diet" was developed to achieve target intakes of 80–120% of the RDA for vitamins A, D, and K, β-carotene, folate, zinc, iron, and calcium, and at the same time meet the different total energy needs of the individual male and female subjects. The core diet, which included the EPG food vehicles, provided 2200 kcal of energy per day.

Because the core diet may not have satisfied the energy needs of all subjects in the study, 6 variations of the "core diet" were used to adjust energy intake by ±200 kcal of energy per day. Each of the 6 variations of the "core diet" included the food vehicles. Subjects with lower energy needs and micronutrient recommended dietary allowances (RDA) received smaller portions of the core diet that provided 1800–2000 kcal of energy per day. Subjects with higher energy needs and micronutrient RDAs were given larger portions of the core diet that provided 2400–3000 kcal of energy per day. Using this approach, the intakes of nutrients of interest were controlled, while providing essentially *ad libitum* intake of energy.

In addition, subjects were weighed on a weekly basis to check the need for adjustment of their dietary intake. Subjects were fed to maintain enrollment weight (±5%) throughout the study. Subjects were also asked to report feelings of hunger or excessive fullness during the study, and calories were adjusted based on this subjective evaluation.

The (7-day rotating) menu provided approximately 35–40% of calories from fat, 15% from protein, and 50% from carbohydrate. The diets were formulated to ensure that the total digestible fat content was comparable across the 4 study groups. The 35–40% fat level was the lowest practically achievable because of the need to supplement the EPG-containing diets with 10, 25, or 40 g/day of regular triglyceride fats (*e.g.*, margarine) to match the fat content of the control diet. In other words, the triglycerides replaced by EPG in muffins, biscuits, cookies, and margarine were supplemented by adding margarine in other parts of the diet. For example, compared to the control group, the 10 g/day EPG study group consumed 10 g/day less of ordinary triglyceride fat because it had been replaced by the EPG in the select dietary food vehicles; therefore, an additional 10 g/day of triglycerides was added elsewhere in the daily menu to keep the triglyceride levels equivalent to the control group. The diets for the 25 and 40 g/day EPG study groups were adjusted in the same manner.

The menu targeted between 80 and 120% of the RDA for vitamins A, D, and K, β-carotene, folate, zinc, and calcium. The levels of vitamin B_{12}, vitamin E, and phosphorus were consistent across study groups. A vitamin D_2 supplement (ergocalciferol, 400 IU) was provided to each subject every morning.

In order to remain eligible, subjects were expected to consume a minimum of 90% of the scheduled study meals. No more than six consecutive study meals could have been missed at any given time during the study without approval from the study director. Subjects were not allowed to miss dinner on the day immediately prior to blood/urine sampling.

Alcohol intake was discouraged and was documented by a dietitian during daily interviews, along with consumption of any other non-study food or drink. The portion size and nutrient value of any such food or drink was assessed by the dietitian using the Minnesota Nutrition Data System, version 2.9.

2.5. Measurement schedule

All subjects began the study on the same calendar day, except for 31 subjects that began within 2 days thereafter. For the purposes of limiting endogenous synthesis of vitamin D_3, exposure of subjects to sunlight was limited by conducting the study in Chicago during the mid-late winter months.