The Preparation of Polyglycerol Esters Suitable as Low-Caloric Fat Substitutes

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Medicinal research has linked dietary fats with such maladies as cancer, heart disease and stroke. The overconsumption of fats has been declared one of the major dietary health concerns in the United States by the Surgeon General. As a result, there is an increased awareness by consumers of their need to reduce the intake of calories derived from fat. The food industry has shown much interest in the development of substitutes for dietary fats and oils. To date, no substitute that can be used as a full fat replacement has entered the marketplace. Linear polyglycerols (LPGs) have been prepared by a proprietary polymerization process. Fatty acid esters prepared from LPGs were found to resist hydrolysis by digestive enzymes and were poorly absorbed in animal feeding tests. When esterified with fatty acids, LPG esters are similar to natural triglycerides in color, odor, taste and other physical characteristics. These properties make LPG oils good candidates for use in nonnutritive edible oil applications, particularly in uses that require stability at high temperatures.

KEY WORDS: Fat substitute, glycidol, low-caloric oils, polyglycerol, polyglycerol esters, polymerization.

The United States and other developed nations are faced with health concerns stemming from the relatively affluent lifestyles prevalent in these countries. Over 30% of the United States population is overweight. Over 50 million people in the United States are estimated to be on some sort of dietary program. These facts point out the need to reduce calorie consumption, and the consumers' increased awareness of this need. However, instead of reducing the quantity of food consumed, many Americans opt to buy specialty foods with lower caloric value.

Of the calories consumed in an average American diet, 40% are derived from fats and oils—a significant increase over the amount consumed in the 1920s. Medicinal research has linked dietary fats with such maladies as cancer, heart disease and stroke. For these reasons, C. Edward Koop, surgeon general of the Reagan administration, declared the overconsumption of fats one of the major dietary health problems in the United States.

The food industry has shown much interest in the development of substitutes for dietary fats and oils because of the large profit potential of such products. The volume of reports in the literature demonstrate that research activity is high (1–10). The successes of sugar substitutes (*e.g.,* saccharin and NutraSweet®), diet beverages and dietetic food preparations have been noted. Several technologies aimed at the reduction of fat intake have been introduced to the consumer [*e.g.,* Simplesse® (2), polydextrose (3)]. None, however, can be employed as a full fat substitute (*i.e.,* one that can be used to replace fats and oils in all applications). This is especially true of oils used in cooking and frying applications.

While the Food and Drug Administration (FDA) continues its evaluation of Procter & Gamble's Olestra® fat substitute, other companies continue their efforts to develop the elusive product(s) that will mimic the physical and sensory characteristics of naturally occurring oils. In addition to sucrose polyesters, other technologies of note are polydimethylsiloxanes (4), dialkylmalonates (5) and polycarboxylic acid esters (6).

Polyglycerol (PG) esters have also been touted as replacements for fats. Although PG esters have been approved as additives by the FDA, the use of PG esters in food preparations at higher levels has been limited due to the odor, bitter taste and dark color characteristic of PG produced *via* conventional methods. These problems may have been overcome by special purification techniques (11). Studies demonstrate, however, that conventional PG esters are metabolized as efficiently as triacylglycerides (12,13). On the basis of these results, the use of conventional PG esters as fat replacements does not appear to be a viable application. However, the fatty acid esters of linear polyglycerols (LPGs) are viable fat substitutes for reasons discussed below.

It is known from studies of the digestive process that the rate of enzymatic hydrolysis of the secondary ester site of triglycerides is slower than at the two primary ester sites (14). Advantage was taken of this selectivity by designing an LPG with enhanced content of secondary hydroxyls (15). Oils prepared from LPGs were much more resistant to enzymatic hydrolysis than natural oils. Animal studies demonstrated that oils derived from LPGs were recovered from feces at a level comparable to mineral oil. The difference in the activity of conventional PG oils *vs.* LPG oils can be ascribed to the higher percentage of secondary ester linkages in the latter.

EXPERIMENTAL PROCEDURES

Materials. Glycidol (Aldrich, Milwaukee, WI); dihydropyran (Aldrich), oleoyl chloride (Aldrich), pyridine (Aldrich), methylene chloride (Fisher, Fairlawn, NJ), KOH (Fisher), NaOH (Fisher), hexane (Fisher), glycerol (Dow Chemical, Freeport, TX), pyridinium *p*-toluene sulfonate (PPTS) (16) were all used as received.

Nuclear magnetic resonance (NMR) experiments. PG samples were dissolved in D_2O with added chromium acetoacetenoate (to suppress the nuclear Overhauser effect). Spectra were obtained on a JEOL GX-270 NMR Spectrometer (Tokyo, Japan). Resonances at 65 and 69 ppm were assigned as primary carbinols. Resonances at 71.7 and 73.3 ppm were assigned as secondary carbinols. ^{13}C-NMR resonances were assigned based upon a mathematical model equation (17). ^{1}H-NMR spectra were obtained on a Varian T-60 NMR Spectrometer (Palo Alto, CA).

Gel permeation chromatography (GPC) analyses. PG samples were dissolved in water/methanol solution and analyzed on a Beckman Sperogel TSK column (2000 PW, 7.5 × 300 mm) (Fullerton, CA) on a Waters Model 510 LC system with a Waters 410 differential refractive index detector (Milford, MA).

Infrared spectra. Infrared spectra were obtained with a Nicolet 510 FTIR Spectrometer (Madison, WI).

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Preparation of linear octaglycerol. Glycidol (675.5 g) was added at a rate of 0.4 mL/min to a glycerine/KOH mixture (64.56 g, 3 mol %) and stirred for several hours at 120–125°C. The resultant polymer had a number average molecular weight (M_n) of 613. The secondary hydroxyl content was 72%, as determined by ^{13}C-NMR analysis.

Preparation of glycidyl-tetrahydropyranyl ether (GTHPE). Dihydropyran (375 mL, 4.11 mol) and PPTS (149 g, 0.594 mol) were dissolved and stirred (37°C) in 900 mL of dry methylene chloride (previously distilled over calcium hydride). PPTS was prepared from pyridine and *p*-toluene sulfonic acid *via* the method of Miyashita *et al.* (16). Glycidol (125 mL, 1.88 mol) was added to the solution over a 45-min period, and the mixture was stirred for 18 h at 37°C. The mixture was concentrated under reduced pressure, and the yellow residue was extracted with several portions of petroleum ether. The ether portions were combined and stripped on the rotary evaporator. Residual volatiles were removed *via* nitrogen sparging. GTHPE was distilled at 59–60°C (0.20 mm Hg). Yield of distilled product was 100 g (33.6% yield) of 97.4% pure material, as determined by gas chromatography (GC): ^{1}H-NMR (CCl_4) – 4.60 ppm (1H); 4.20 – 2.30 ppm (7H, m); 1.34 ppm (6H, *bs*); Infrared (IR) (neat film)—910 cm^{-1} (strong); no absorption at 1610 cm^{-1}; no absorption above 3000 cm^{-1}.

Preparation of branched octaglycerol. A mixture of glycerol (5.52 g, 0.06 mol) and KOH (0.3 g, 5.4 mmol) was heated and stirred (80°C, 6 mm Hg) until the mixture was homogeneous. Atmospheric pressure was restored, and GTHPE was added over an 8 h period at 125–135°C. The mixture was allowed to stir at 100°C for 10 h after the addition was completed. The poly-GTHPE was cooled to room temperature and stirred in 200 mL of 1 N HCl for 3 h. The pH of the solution was raised to 6 with 10 N KOH, and water was stripped under reduced pressure. The residue was dissolved in a mixture of acetone and methanol, then filtered from precipitated KCl. The solvent was removed under reduced pressure, and residual water was azeotropically distilled with toluene. GPC analysis revealed the presence of residual glycerine. The polymer had a M_n of 587. Primary hydroxyl content was determined to be 75% by ^{13}C-NMR analysis.

Octaglycerol via *glycerol condensation.* Glycerol (500.68 g, 5.44 mol) was mixed with NaOH (4.85 g, 0.121 mol), stirred and heated to 230–250°C for 26 h, with a slight nitrogen purge and reduced pressure. Volatiles were taken overhead during the heating period. The polyol had a M_n of 625. Secondary hydroxyl content was 41%.

Preparation of linear octaglyceroldecaoleate, LPG oil. A 5-L round-bottom flask, fitted with a constant-addition funnel and an overhead motorized stirrer, was charged with octaglycerol (188.8 g, 0.325 mol) and pyridine (262 g, 3.3 mol) under a blanket of nitrogen. The contents of the flask were stirred vigorously. The constant addition funnel was charged with freshly distilled oleoyl chloride (180–200°C, 2 mm Hg) and blanketed with nitrogen. Oleoyl chloride (987.6 g, 3.3 mol) was dripped into the polyol mixture, such that the temperature was maintained below 70°C. Hexane (1 liter) was added to the heterogeneous mixture to aid dispersion of the reactants. The mixture was stirred for 3 h after all acid chloride was added, then filtered through glass wool and a sintered glass funnel of medium porosity. The decaoleate was concentrated on the rotary evaporator, combined with an equal volume of water, and a crude "steam-stripping" was carried out by removal of the water under reduced pressure. The product was saturated with ethanol and then extracted with additional ethanol until a level of less than 0.1% free fatty acid was obtained. The alcohol was removed under reduced pressure. Residual volatiles were completely removed by twice carrying out the "steam-stripping" procedure described previously.

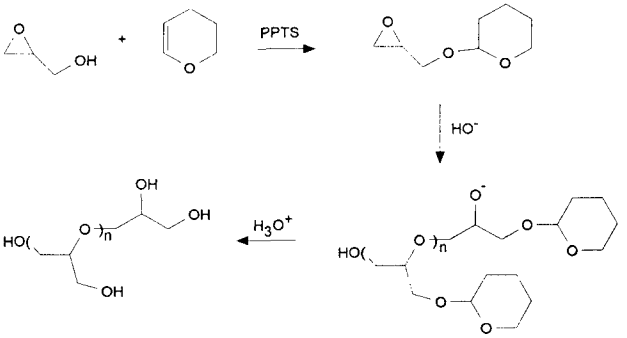
Fecal analyses. Feces were collected, weighed and extracted with a lipophilic solvent. Fecal oil content was determined by weight difference before and after extraction.

RESULTS AND DISCUSSION

Linear octaglycerol was prepared *via* the alkaline polymerization of glycidol, exercising strict control of the reaction parameters. For purposes of comparison, branched octaglycerol was prepared *via* the polymerization of glycidyl-tetrahydropyranyl ether (Scheme 1). Octaglycerol was also targeted *via* the conventional method of glycerol condensation in the presence of sodium hydroxide at a temperature greater than 230°C (11). Each of the polymers was analyzed by GPC for molecular weight and by ^{13}C-NMR for primary and secondary hydroxyl content.

Results of the GPC analyses show glycidol polymerization afforded much better control of M_n than did the glycerine condensation method (Table 1). The M_ns of LPGs prepared by glycidol polymerization were controlled to within ±1 glycerine unit of the target. The fraction of polyol within the desired M_n range was generally greater than 90%, and the polydispersivity (a measure of polymer uniformity) of LPGs was ordinarily close to unity. This was advantageous in that the lower M_n oligomers, which are more effectively metabolized by lipase, were nearly eliminated in LPGs. The GPC of branched PG consisted of two well-resolved peaks of M_n 587 and 92. The latter was assumed to be residual glycerol. As shown in Table 1, the glycerine condensation route produced a conventional PG mixture with a wide M_n distribution, including a significant amount of residual glycerine. PG isolated from a commercial decaglycerol fatty ester had a similarly wide M_n range.

LPG was analyzed by NMR and contained 72% secondary hydroxyls (theoretical max = 80%). The high



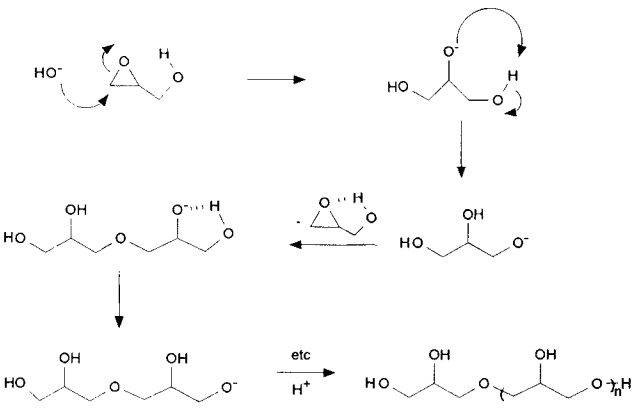
SCHEME 1

TABLE 1

Molecular Weight Comparison of Polyglycerols

	LPG[a]	BPG[b]	PG[c]
Molecular weight of total polymer (M_n)	555	264	336
M_n of major fraction	613	587	625
Area % major fraction	94	85	62
Polydispersivity[d] (M_w/M_n)	1.140	1.858	1.523

[a]Linear polyglycerol.
[b]Branched polyglycerol.
[c]Conventional polyglycerol.
[d]A polymer is monodisperse if M_w/M_n = 1.000 (20). M_w is weight avg. mol wt.; M_n, number avg. mol wt.

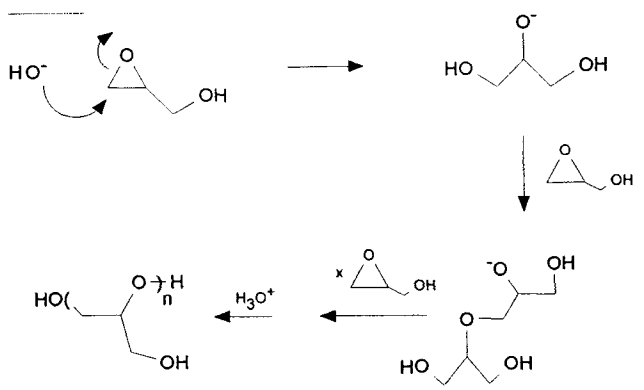


SCHEME 3

percentage of secondary hydroxyls obtained *via* the polymerization of glycidol cannot be explained through a simple ring-opening polymerization mechanism, which would lead to the branched product (Scheme 2). The product can be explained, however, if ring-opening is followed by a proton transfer to form the primary alkoxide, which then acts as the nucleophile (Scheme 3). The proton transfer may be facilitated by intramolecular hydrogen bonding, although this is not a necessary feature of the proposed mechanism. Reaction conditions were carefully chosen to maximize the formation of the linear product.

Analysis of branched PG by ^{13}C-NMR spectroscopy showed that it contained 75% primary hydroxyls (theoretical maximum = 80%). In this sequence, polymerization of GTHPE can proceed only through the secondary alkoxide and should yield—with the exception of the terminal groups—all primary hydroxyls. Departure from the theoretical composition was due to the presence of glycerol, which formed as a result of the hydrolysis of residual GTHPE.

The glycerol condensation method was not as selective a process as the glycidol polymerization and resulted in a primary/secondary hydroxyl ratio of approximately 1:1. Conventional PG contained 41% secondary hydroxyls. Residual glycerol and lower M_n oligomers were present in the polymer mixture, and this was reflected in the analysis. PG isolated from a commercial source had 49% secondary hydroxyls and, therefore, is similar to PG prepared by the conventional process.



SCHEME 2

The high degree of polymerization of LPGs, in conjunction with hydrogen bonding between polymer chains, resulted in high viscosities at ambient temperature. The viscosity difference was apparent on comparison with conventional PG. The viscosity of linear decaglycerol, for example, could not be measured at 25°C by ASTM D-445 (18) because the polymer behaved much like an amorphous solid. The viscosity of decaglycerol measured at 35°C was approximately 323,000 centiStokes. Even though working with the polyol was difficult at room temperature, warming the LPG alleviated problems caused by high viscosity. The color of LPG was Gardner 6 without processing. There was no distinct odor associated with the product prepared in the manner described here.

Linear, branched and conventional octaglyceroldecaoleates were prepared by using identical procedures. PG oils prepared for feeding studies were processed to free fatty acid values of less than 0.1%. In addition to being treated to reduce free fatty acids, oils evaluated in applications and stability tests were also bleached. Steam-deodorization was conducted according to a laboratory procedure outlined by Bitner *et al.* (19).

In an animal screening test, 80% of the LPG oil fed was recovered in the feces. This compared favorably to the amount of mineral oil recovered (85%) by the same screening procedure. Except for somewhat higher viscosities, the physical characteristics and thermal stability of LPG oils were nearly identical to those of triglycerides. The virtual absence of esters derived from lower oligomers in LPG oils rationalizes their higher viscosity, compared with conventional PG esters. However, blends of LPG oils with triglycerides yield oils with viscosities near those of the triglycerides.

LPG oils may derive some advantage over other fat substitutes by virtue of the current use of conventional PG oils as additives in the food industry. Several studies of the digestion of conventional PG oils have been reported in the literature (12,13). These studies have concluded that enzymatic hydrolysis of conventional PG oils mirrors that of triglycerides. A radio-labeling study demonstrated that the fatty acids liberated upon hydrolysis are utilized in a normal fashion, and that PG is excreted unchanged in the urine (13). The metabolites of PG oils, therefore, are safe and nontoxic. Conventional PG and oils derived from

conventional PG were granted the GRAS (generally recognized as safe) distinction by the FDA and have had this status for more than thirty years.

Another possible advantage of LPG oils is that, unlike sucrose polyesters, LPG oils are not inert to enzymatic hydrolysis. While they resist the action of lipolytic enzymes, they eventually can be broken down. Thus, if small amounts of LPG oils are absorbed, they should undergo the same metabolic fate as conventional PG oils over an extended period of time.

The FDA approval will be required for LPG oils, because the proposed application may result in use of this material in the food chain at levels unanticipated by the FDA thirty years ago. Further study of the dietary effects of LPG oils, therefore, is necessary before they find widespread use.

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