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Development of new tissue conditioner using acetyl tributyl citrate and novel hyperbranched polyester to improve viscoelastic stability

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ARTICLE INFO

Article history:
Received 27 February 2015
Accepted 24 March 2015

Keywords:
Viscoelasticity
Acetyl tributyl citrate
Hyperbranched polyester
Tissue conditioner

ABSTRACT

Objective. The objective was to develop a new tissue conditioner using acetyl tributyl citrate (ATBC), tributyl citrate (TBC), and a novel hyperbranched polyester (TAH) with long-term stable viscoelasticity.

Methods. Plasticizers, i.e., ATBC, TBC, TAH (number-average molecular weight, 1306 g/mol; weight-average molecular weight, 4245 g/mol), butyl phthalyl butyl glycolate (BPBG), dibutyl phthalate (DBP), benzyl benzoate (BB), Shofu Tissue Conditioner II (Shofu), and GC Soft-Liner (GC), in nine combinations (ATBC + TAH, TBC + TAH, ATBC, TBC, BPBG, DBP, BB, Shofu, and GC), with gelation times between 120 and 180 s were used; Shofu and GC were used for comparison. The dynamic viscoelasticity properties, i.e., shear storage modulus (G'), shear loss modulus (G''), loss tangent ($\tan\delta$), and complex dynamic shear modulus (G^*) were determined at 37 °C, using a rheometer, after immersion in water for 0, 1, 3, 7, 14, and 28 d. The surface hydrophobicity was examined using a static contact angle analyzer, and the biocompatibility was evaluated using a 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide assay. Weight changes, solubility, and water absorption were measured using an analytical balance.

Results. TAH addition increased the viscoelastic stability; ATBC + TAH was the most stable among the tested groups. TAH decreased the contact angle and increased the water absorption, but decreased the ATBC solubility. The ATBC + TAH group biocompatibility was similar to those of the control group.

Significance. The developed ATBC + TAH plasticizer has potential applications as a new tissue conditioner. Its clinical efficacy needs to be evaluated in clinical trials.

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http://dx.doi.org/10.1016/j.dental.2015.03.012
0109-5641/

1. Introduction

Viscoelastic tissue conditioners are generally used in edentulous patients to treat lesions resulting from ill-fitting dentures, or as functional impression materials to record the dynamic form of the edentulous ridge [1]. The long-term stability of the viscoelasticity and dimensions is therefore important in the clinical use of tissue conditioners [2,3]. Tissue conditioners consist of a powder and a liquid. The powder is typically poly(ethyl methacrylate) (PEMA), and the liquid usually contains ethanol and an ester plasticizer such as butyl phthalyl butyl glycolate (BPBG), dibutyl phthalate (DBP), or benzyl benzoate (BB) [4,5]. A major disadvantage of tissue conditioners is leaching of the plasticizer and ethanol within the first 24–48 h of use, which causes rapid loss of viscoelasticity during clinical use [6,7]. These viscoelastic changes may irritate denture-bearing areas and cause damage to edentulous soft tissue that has just healed after use of the tissue conditioner. Such materials therefore have to be replaced at short intervals, which is time consuming and costly for both dentists and patients.

Several methods for improving the viscoelasticity of tissue conditioners have been studied. The first is addition of poly(methyl methacrylate) (PMMA) to PEMA as a retarder. The results showed that addition of 10 wt% PMMA gave the most stable dynamic viscoelasticity and the lowest leaching of plasticizer [8]. The molecular weight of the plasticizer affects its leaching into the oral cavity [6]; the leaching of a low-molecular-weight plasticizer such as BB is greater than those of high-molecular-weight plasticizers such as BPBG and DBP [3]. The second method is to change the plasticizer. One study showed that replacement of the conventional powder and plasticizer with poly(*n*-butyl methacrylate) and di(2-ethylhexyl) maleate improved the durabilities of tissue conditioners [3]. The third method used coated alcohol-free tissue conditioners; the viscoelastic properties of these were superior to those of conventional materials containing ethanol [9].

In addition to having stable viscoelasticity, materials must be biocompatible. A study has shown that some phthalate esters (e.g., BPBG and DBP), which are added to tissue conditioners as plasticizers, have estrogenic activity [10]. An ideal tissue conditioner should therefore provide long-term stability of the viscoelasticity properties, and its components should have biocompatibility. Acetyl tributyl citrate (ATBC) and tributyl citrate (TBC) are produced from the natural compound citric acid. They are non-toxic, and have been used in personal care, the food industry, and as plasticizers in polylactides [11,12]. In this study, a novel tissue conditioner was developed by adding a hyperbranched polyester (TAH) to ATBC and TBC. The viscoelastic properties of the obtained conditioners were highly stable compared with those of conditioners obtained using three conventional plasticizers (BPBG, DBP, and BB), and two commercial products [Shofu Tissue Conditioner II (Shofu) and GC Soft-Liner (GC)]. The dynamic viscoelasticity properties [shear storage modulus (G'), shear loss modulus (G''), loss tangent ($\tan\delta$), and complex dynamic shear modulus (G^*)], surface hydrophobicity, weight changes, solubility, water absorption, and biocompatibility were investigated.

2. Materials and methods

2.1. Materials

PEMA [weight-average molecular weight (M_w): 850,000 and particle size 35–45 μm], ATBC (M_w: 402.48), TBC (M_w: 360.44), BPBG (M_w: 336.38), DBP (M_w: 278.34), BB (M_w: 212.24), ethanol (≥99.8%), adipic acid, heptanoic acid, trimethylamine, trimethylolpropane triglycidyl ether, and tetrahydrofuran were purchased from Sigma-Aldrich (St. Louis, MO, USA), and used without further purification. TAH (8.7 wt%) was added to ATBC and TBC to improve the stability of the viscoelasticity. Shofu (Shofu, Inc., Kyoto, Japan) and GC (GC Co., Tokyo, Japan) were used for comparison. Table 1 lists the components and powder/liquid (*P*/*L*) ratios of the experimental mixtures and Fig. 1 shows the chemical structures of the plasticizers.

2.2. TAH synthesis

Adipic acid and heptanoic acid were added to a batch reactor, and trimethylamine was added to the mixture as a catalyst. The mixture was stirred to obtain a homogenous solution. Trimethylolpropane triglycidyl ether was then added to the solution; the molar ratios of adipic acid, heptanoic acid, and trimethylolpropane triglycidyl ether were 1:0.75:1.5. Polymerization was performed at 120 °C for 2 h and then 140 °C for 12 h. The product was dissolved in tetrahydrofuran, and the molecular weights of TAH were determined using a gel permeation chromatograph (GPC) (HLC-8320GPC EcoSEC, Tosoh Corp., Tokyo, Japan) coupled with two columns, which were calibrated with polystyrene standards. The number-average

Table 1 – Components of nine formulations.

Code	Powders	Liquids	*P*/*L* by weight
ATBC + TAH	PEMA 100 wt%	ATBC 78.3 wt% + TAH 8.7 wt% + EtOH 13 wt%	1.2
TBC + TAH	PEMA 100 wt%	TBC 78.3 wt% + TAH 8.7 wt% + EtOH 13 wt%	1.2
ATBC	PEMA 100 wt%	ATBC 90 wt% + EtOH 10 wt%	1.2
TBC	PEMA 100 wt%	TBC 90 wt% + EtOH 10 wt%	1.2
BPBG	PEMA 100 wt%	BPBG 95 wt% + EtOH 5 wt%	1.2
DBP	PEMA 100 wt%	DBP 95 wt% + EtOH 5 wt%	1.2
BB	PEMA 100 wt%	BB 98 wt% + EtOH 2 wt%	1.2
Shofu	PEMA 100 wt%	DBP 87 wt% + EtOH 13 wt%	1.2
GC	PEMA 100 wt%	DBP 4.3 wt% + BPBG 80.9 wt% + EtOH 14.8 wt%	1.2