Brazilian Dental Journal (2018) 29(1): 48-53
http://dx.doi.org/10.1590/0103-6440201801441
ISSN 0103-6440

Pentaerythritol Tetrasalicylate in the Chemical Composition of Root Canal Sealers

Manuela Gonçalves de Souza e Silva[1], Eliseu Aldrighi Münchow[1], Rafael Pino Vitti[2,3], Mário Alexandre Coelho Sinhoreti[3], Evandro Piva[1], Fabrício Aulo Ogliari[4], Cesar Henrique Zanchi[1]

[1]Department of Operative Dentistry, School of Dentistry, UFPel - Universidade Federal de Pelotas, Pelotas, RS, Brazil
[2]Department of Prosthodontic, School of Dentistry, UNITAU - Universidade de Taubaté, Taubaté, SP, Brazil
[3]Department of Restorative Dentistry, Piracicaba Dental School, UNICAMP - Universidade de Campinas, Piracicaba, SP, Brazil
[4]Department of Polymeric Materials, School of Engineering and Materials Science, UFPel - Universidade Federal de Pelotas, Pelotas, RS, Brazil

Correspondence: Cesar Henrique Zanchi, Rua Gonçalves Chaves, 457, 96015-560 Pelotas, RS, Brasil. Tel: +55-53-3225-674. e-mail: chzanchi@gmail.com

The aim of this study was to synthesize and evaluate physicochemical properties of a new salicylate derivative in experimental calcium-based root canal sealers. Two salicylate derivatives were synthesized for the transesterification reaction of methyl salicylate with two different alcohols (1,3-butylenoglicol disalicylate-BD and pentaerythritol tetrasalicylate -PT) in molar ratio 1:3 and 1:6, respectively. The products (BD and PT), were characterized by Fourier Transform Infrared Spectroscopy (FTIR) and Nuclear Magnetic Resonance spectroscopy (RMN). Calcium-based experimental sealers were prepared with the same catalyst paste (60% of MTA, 39% of n-ethyl-o-toluenesulfonamide, and 1% titanium dioxide) and four different concentrations of BD and PT in the base pastes (40/0 - control, 35/5, 30/10 and 20/20) with 60% of bismuth oxide. The experimental sealers were evaluated for setting time, solubility (24 h, 7, 14 and 30 days), diametral tensile strength and Young's Modulus. Data were analyzed by one- or two-way ANOVA with Tukey's test ($p<0.05$). The addition of PT reduced the materials setting time. After 24 h the sealer 40/0 and 35/5 had higher solubility, and after 14 and 28 days the sealer 20/20 showed the lowest solubility ($p<0.05$). After 7 days the sealer 20/20 stabilized its solubility. The sealer 40/0 presented the highest values and the 20/20 presented the lowest values of diametral tensile strength and Young's modulus ($p<0.05$). The addition of PT to calcium-based root canal sealers provides benefits to the setting time and solubility.

Key Words: mineral trioxide aggregate, root canal sealer, salicylate resin.

Introduction

Different techniques can be used for endodontic filling, and most them use gutta-percha points associated with endodontic sealers. In addition, many types of root canal sealers are available in the market with different physicochemical and biological properties (1,2). Generally, such materials are classified into four groups according their chemical compositions: zinc oxide-eugenol, glass ionomer, resin and calcium based sealers (1-3).

Recently, special attention has been given to calcium hydroxide-based sealers and its action mechanism, which promotes periapical tissue repair. Due to their biological properties, this type of root sealer is capable to release calcium ions and hydroxyls that increase the pH (4-8) and induces the repair of the affected area through the neo-tissue formation (9). Although calcium-based sealers present excellent biological properties, several studies have reported their high solubility (8,10) and weak or no adhesion to dental tissues (11), factors that determine the outcome of root canal treatment. In attempt to overcome these drawbacks, low solubility calcium alternative sources, such as mineral trioxide aggregate (MTA) have been tested as components of new endodontic sealers (7,8,12). The advantage of replacing the calcium hydroxide by MTA is the possibility to control or, at least, to reduce the excessive solubility of currents sealers without loss the desirable biological properties (13).

Besides the possibility to change the calcium source, modifications in the salicylate resin can be performed. Salicylate resin has been used as resin matrix for endodontic sealers since 1999 (14,15). The chemical structure of salicylate derivatives used in the composition of endodontic sealers has direct influence on the properties of the polymer formed during and after the cure (8). Endodontic sealers that contain salicylate resin presented satisfactory physicochemical (16) and cytotoxicity (17) properties. However, salicylate based sealers have high solubility and water absorption (8) jeopardizing the treatment longevity. Although the butylenoglicol disalicylate (BD) is the salicylate resin traditionally employed in the commercial calcium-based root canal sealers (8,16), others salicylate derivatives as pentaerythritol tetrasalicylate (PT) showing higher functionality should be tested and employed in attempt to produce more stable and less hydrophilic polymers. There is a lack of knowledge regarding the effects of different salicylate resins as BD and PT on the properties of the cements. Thus, it would be interesting to investigate experimental endodontic sealers based on

PT in attempt to improve physicochemical and biological properties of the cements.

The aim of this study was to synthesize a new salicylate derivative (PT) and evaluate physicochemical properties of experimental calcium-based root canal sealers made with this salicylate derivative. The hypothesis was that the changes in the molecular structure of salicylate derivatives would result in different physicochemical characteristics of the polymer.

Material and Methods

Synthesis of Salicylate Derivatives

Two salicylate derivatives were synthesized by transesterification of methyl salicylate (Synth Laboratory, São Paulo, SP, Brazil) with two different alcohols, BD and PT, in a molar ratio of 1:3 and 1:6, respectively (Fig. 1). The isopropoxide titanium (Sigma-Aldrich, St. Louis, MO, USA) was used as a catalyst agent. The reaction was maintained at 200 °C for 2 h. The products were purified by vacuum distillation and characterized by Fourier Transform Infrared Spectroscopy (FTIR) and Nuclear Magnetic Resonance spectroscopy (NMR) (Fig. 2).

Experimental Endodontic Sealers Formulation

Four experimental calcium-based root canal sealers were formulated in two pastes: base and catalyst. The catalyst paste was the same for all sealers, composed by 60% of MTA (Angelus, Londrina, Brazil), 39% of n-ethyl-o-toluenesulfonamide and 1% titanium dioxide. Four base pastes were formulated with different concentrations of BD and PT (Table 1).

The handling of all sealers was performed by mixing equal portions of the two pastes. For every gram of handled material 10 µL of distillated water was added to the mixture, according to the International Organization for Standardization (18).

Setting Time Test

Six specimens with an internal diameter of 10 mm and a thickness of 2 mm were prepared for each experimental sealer. A Gilmore-type needle with weight of 100 ± 0.5 g with a tip of 2.0 ± 0.1 mm in diameter was used to determine the initial setting time. Another Gilmore-type needle weighing 456 ± 0.5 g and a tip of 1 ± 0.1 mm in diameter was used to determine the final setting time. The needles were carefully placed vertically on the sample surface. The needle tip was cleaned and the probing was repeated until the indentations could not be observed on the sealer surface. The setting time test was performed with evaluations performed every 3 min during the first half hour, every 5 min for the next 90 min, and every 15 min thereafter until the setting time was approached (initial setting). The analysis continued every 15 min until the establishment of the final setting (19).

Table 1. Composition of base pastes evaluated in this study

Base Paste	Bismuth	Butylenoglicol disalicylate	Pentaerythritol tetrasalicylate
20/20	60%	20%	20%
30/10	60%	30%	10%
35/5	60%	35%	5%
40/0 (control)	60%	40%	0%

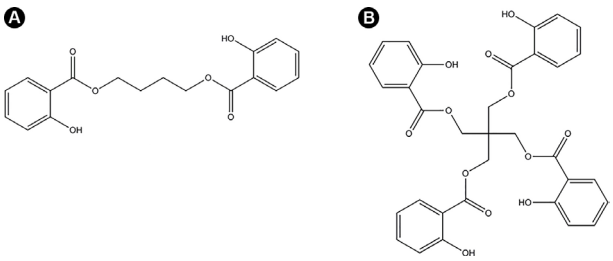

Figure 1. A: Butylenoglicol disalicylate molecular structure. B: Pentaerythritol tetrasalicilate molecular structure.

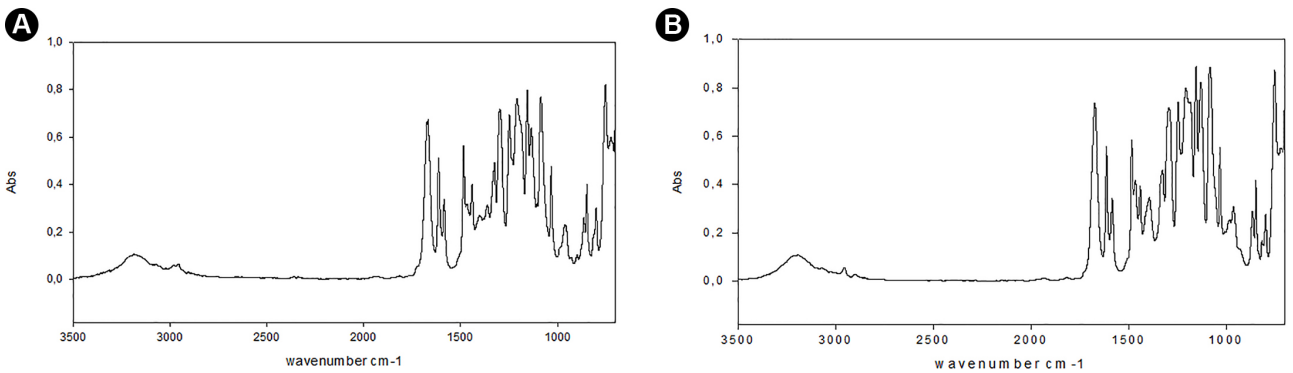

Figure 2 A: FTIR spectra from butylenoglicol disalicylate. B: FTIR spectra from pentaerythritol tetrasalicylate.

Solubility

Cylindrical molds with 6.32 mm internal diameter and 1.5 mm thickness were used to prepare the specimens (n = 12). The size of the specimens and the amount of water used was modified as proposed by Carvalho-Junior et al. (20). The mold was positioned over a glass slide and then filled with the experimental sealer. The assembly was placed in an incubator (37 °C, 95% relative humidity) for 24 h. Then the specimens were removed from the mold and weighed three times each with an accuracy of 0.0001 g to determine the initial mass. The specimens were suspended by a metal thread and placed inside a plastic container containing 10 mL of distilled water, to avoid that any surface of the specimen came into contact with the container. The sealed containers were stored for 24 h, 7, 14 and 28 days at 37 °C. After these periods, the specimens were removed from the containers, rinsed with distilled water, blotted dry with absorbent paper, placed in a desiccator for 24 h, and then reweighed three times each to determine the final mass. The solubility was calculated by the difference between the final mass and the initial mass, expressed as the percentage of the original mass.

Diametral Tensile Strength and Young's Modulus

Ten cylindrical specimens were made of each experimental sealer, using a mold with 4.0 mm internal diameter and 2.0 mm thickness (21). The mold was positioned over a glass slide and filled with the experimental sealer. Then, the assembly was placed in an incubator (37°C, 95% relative humidity) for 24 h. After this period, the material was removed from the mold and the specimens were subjected to a compressive load (10 KN) in a universal testing machine (DL-500, Emic, São José dos Pinhais, PR, Brazil) at a crosshead speed of 0.5 mm/min until fracture.

Statistical analysis

Data for setting time, diametral tensile strength and Young's modulus were analyzed by one-way ANOVA and Tukey's test ($p<0.05$). Data for solubility were analyzed by two-way ANOVA (sealer and storage time factors) and Tukey's test ($p<0.05$).

Results

The salicylate derivatives syntheses were confirmed by FTIR and NMR. At room temperature the products showed different rheological characteristics, the BD was liquid and the PT was solid.

The setting time of experimental sealers evaluated in this study are showed in Table 2. The addition of pentaerythritol tetrasalicylate reduced the materials setting times ($p<0.05$). Regarding to initial setting time, the sealer 40/0 presented the highest time, the sealers 35/5 and 30/10 similar ($p=0.811$) intermediates times, and the 20/20 present the lowest time values ($p<0.05$). Concerning the final setting time, the sealer 40/0 present the highest time, the sealer 20/20 the intermediate time, and the sealers 35/5 and 30/10 present similar ($p=0.205$) and lowest final setting time.

The solubility of experimental materials is presented in the Table 3. After 24 h the sealer 40/0 and 35/5 had higher solubility, after 7 days the sealers did not differ, and after 14 and 28 days the sealer 20/20 showed the lowest solubility ($p<0.05$). After 7 days the sealer 20/20 stabilized its solubility, while the other continued to gradually

Table 2. Mean (and standard deviation) of initial end final setting time

Sealer	Solubility (%)			
	24 h	7 days	14 days	28 days
20/20	3.69 (± 0.23) ^{C,b}	8.42 (± 0.44) ^{A,a}	8.93 (± 0.54) ^{B,a}	9.66 (± 0.47) ^{D,a}
30/10	5.21 (± 0.40) ^{B,d}	8.97 (± 1.96) ^{A,c}	12.54 (± 0.38) ^{A,b}	13.95 (± 0.65) ^{C,a}
35/05	6.85 (± 0.19) ^{A,d}	8.18 (± 0.52) ^{A,c}	13.65 (± 0.76) ^{A,b}	16.59 (± 0.74) ^{B,a}
40/0	5.74 (± 0.25) ^{AB,d}	9.05 (± 0.78) ^{A,c}	12.74 (± 0.63) ^{A,b}	24.14 (± 1.14) ^{A,a}

Data with different superscript capital letters in column and different superscript lowercase letters in row are statistically ($p<0.05$).

Table 3. Mean (and standard deviation) of solubility in different storage

Sealer	Setting time (min)	
	Initial	Final
20/20	86.67 (± 5.58) ^{C}	775 (±7.75) ^{B}
30/10	116.67 (± 2.58) ^{B}	550 (± 12.25) ^{C}
35/5	114.17 (± 3.76) ^{B}	560 (± 7.75) ^{C}
40/0	412.5 (± 8.22) ^{A}	803.33 (± 4.08) ^{A}

Data with different superscript letters are statistically different ($p<0.05$).

Table 4. Mean (and standard deviation) of diametral tensile strength and Young's modulus

Sealer	Diametral tensile strength (MPa)	Young's modulus (MPa)
20/20	0.37 (± 0.09) ^{C}	9.54 (± 5.27) ^{C}
30/10	1.07 (± 0.16) ^{B}	33.24 (± 11.10) ^{B}
35/5	0.89 (± 0.18) ^{B}	31.10 (± 13.81) ^{B}
40/0	1.43 (± 0.28) ^{A}	49.96 (± 12.68) ^{A}

Data with different superscript letters are statistically different ($p<0.05$).

release its components.

The diametral tensile strength and the Young's modulus of sealers tested are showed in Table 4. The sealer 40/0 presented the highest values and the sealer 20/20 the lowest values of diametral tensile strength and Young's modulus ($p<0.05$). The sealers 30/10 and 35/5 presented similar diametral tensile strength ($p=0.32$) and Young's modulus ($p= 0.968$), which was different and intermediate than the presented by the other sealer ($p<0.05$).

Discussion

All the calcium-based root canal sealers have two active reagents in its compositions, a source of calcium and a salicylate resin (8). During the handling these two components are mixed and the setting reaction starts after placed in the root canals and subsequent contact with the tissue fluids (8). The calcium ions react with the salicylate molecules forming an ionic polymer (8). This reaction is responsible for setting and also to promote physicochemical characteristics to the material (8). Many studies have evaluated different calcium sources in an attempt to solve drawbacks of this type of sealers (7,22), however changes in salicylates resin had not been studied. In this study was hypothesized that changes in the molecular structure of salicylate derivatives results in different physicochemical characteristics of the polymer formed as rheological characteristics, solubility, and strength. The results confirmed the hypothesis.

The salicylate derivatives syntheses were successfully obtained as confirmed by the FTIR and RMN spectrums. It is the first time that a salicylates transesterification reaction is described using titanium isopropoxide as catalyst. This catalyst is extremely safe, therefore it is not necessary to remove the final product, since it decomposes to titanium dioxide which is widely used as white pigment in many dental materials.

The calcium-based endodontic sealers commercially available use in its composition the BD. This salicylate derivative presents functionality 2 and therefore has the ability to form linear or circular polymers (12). This technology was firstly described by Dougherty (23) in a patent document US 3,047,408. Jandourek (24) in a US patent document 4,240,832 used a resinous condensate polysalicylate in the development of dental cements. However, the final product has a melting point below 60°C, then the use of methyl salicylate as a diluent is necessary. The low functionality and molecular mass of the methyl salicylate determines the worst mechanical properties for the material and a greater solubility.

The setting time of a sealer is important to allow adequate working time and proper viscosity to permit the complete filling of the root canal system (12). The addition of PT reduced the materials initial and final setting times. This time reduction could have occurred due the differences in functionality of salicylate derivatives. The PT presents functionality 4, which makes it more reactive than that BD that has functionality 2 (12). The higher reactivity accelerated the setting reaction of materials with PT in its composition. The initial setting time of experimental sealers obtained in this study was in agreement with others studies (8). Although the addition of PT has reduced the setting time, all experimental materials showed viable times for clinical use.

For the solubility test, the size of the specimens was determined in accordance with Carvalho-Junior et al. (20) that proposed to use a matrix smaller than ADA nº 57. The authors concluded that reducing the size of the specimens does not affect the accuracy of the solubility test. However, of all molds tested the authors recommend to use the second mold smaller size (7.75 x 1.5 mm), because the smallest mold size (6.32 x 1.5 mm) resulted in the fracture of some specimens in only one group (eugenol-based cement) (20). In our study, it was used materials (experimental calcium-based root canal sealers based on MTA and salicylate resins) with different chemical composition, structure, and physical properties as cohesive strength. How the main idea of the Carvalho-Junior et al. (20) is to use the smallest volume of endodontic sealers without jeopardize the solubility test, and no fracture occurred in our specimens, we used the matrix with 6.32 x 1.5 mm of dimensions. But, it is important to emphasize that we carefully maintained the ratio density/volume (endodontic sealers/distilled water) proposed by Carvalho-Junior et al. (20). The experimental endodontic sealers used in this study have different density of the materials used by Carvalho-Junior et al. (20). So, to maintain the same ratio density/volume (42.44×10^{-5}) we used 10 mL of distilled water rather than 5 mL.

The experimental endodontic sealers presented higher values of solubility than ISO 6876:2001 recommendation (<3% mass fraction). These data are in accordance with the results of previous reports (8,10,16,19). The addition of PT positively influenced the solubility of experimental sealers. The materials containing larger amount of PT, 30/10 and 20/20, were those with lower solubility in the first 24 h. The addition of 20% of PT was able to stabilize the solubility of the material after 7 days, while the other continued to gradually release its components until the last evaluation period of 28 days. Maybe this phenomenon can be explained by the polymer formed after set, where the larger amount of PT will be formed a polymer heavily cross-linked (rigid and strong), and consequently more stable and less hydrophilic. The differences regarding the solubility may be related to the size of the polymer chain (PT has functionality 4 and BD has functionality 2). A polymer more stable allows the

quality of the filling be preserved, determining factor in the prognosis of endodontic treatment (1-3), since that porosities on endodontic sealers surface facilitate the water absorption over time promoting its solubility (25).

It is important to point out that the high solubility of a canal sealer might result in loss of structure to the oral environment and create lack of integrity in the sealer (25). These spaces might provide a pathway for microorganisms and their toxic products into periapical tissues, damaging the endodontic space (25). Thus, endodontic sealers materials may remain within the root canal and the solubility proposed by ISO 6876:2001 is essential (18). On other hand, calcium ions release is an important property of MTA cements to promote mineralization, cell migration and differentiation in dental tissues (8), and high solubility facilitate the hydration reactions of calcium silicates to produce calcium hydroxide (10). Thus, further studies are necessary to comprise of the advantages of bioactive components released from calcium-hydroxide-based sealers within the root canal. Moreover, the ISO standardized solubility test advises immersion of the endodontic sealers on water after the material reaches setting time of 50% longer stated by manufacturer (18), but clinically the endodontic sealers are immediately placed into contact with moisture of the dental tissues.

The mechanical strength property should be considered in retreatment and posts cementation, cases where is necessary to remove the material inside of root canal, and due its relation to the structural integrity of the material and subsequent sealing of the root system (13). There are no ISO standards for diametral tensile strength. So it is difficult to compare our results with other studies, since each work uses different methodologies (samples size, storage, etc.) and the present study is the first research evaluating calcium-based root canal sealers based on PT. The analysis of the experimental sealers demonstrated that the addition of PT influenced negatively the mechanical strength of materials. This may have occurred because of the limited solubility of PT in BD, which can formed a separation phase and incorporation of defects in the sample. The group with the highest amount of PT and lower BD showed the worst results, while the group without PT showed the highest values for diametral tensile strength and Young's modulus. The sealing of endodontically treated teeth is usually performed by the combination of two materials, the sealer and the gutta-percha cone, however, a sealer mechanical strength may not be its most critical property.

The addition of PT improves setting time and solubility of experimental endodontic sealers. However further studies are required to verify the impact of the PT in the biological and other physicochemical properties of sealer, as pH and calcium ion release.

Resumo

O objetivo neste estudo foi sintetizar e avaliar as propriedades físico-químicas de um novo derivado do salicilato em cimentos endodônticos experimentais à base de cálcio. Dois derivados de salicilato foram sintetizados por meio de uma reação de trans esterificação do salicilato de metila com dois diferentes alcoóis (1,3-butilenoglicol dissalicilato-BD e pentaeritritol tetrassalicilato-PT) na proporção molar de 1: 3 e 1:6, respectivamente. Os produtos (BD e PT), foram caracterizados por espectroscopia infravermelho transformada de Fourier (FTIR) e espectroscopia de ressonância magnética nuclear (RMN). Os cimentos experimentais à base de cálcio foram preparados com a mesma pasta catalisadora (60% de MTA, 39% de N-etil o/p toluenosulfonamida e 1% de dióxido de titânio) e quatro concentrações diferentes de BD e PT nas pastas base (40/0 - controle, 35/5, 30/10 e 20/20) com 60% de óxido de bismuto. Os cimentos foram avaliados quanto ao tempo de endurecimento, à solubilidade (24 h, 7, 14 e 28 dias), resistência à tração diametral e ao módulo de elasticidade. Os dados foram analisados por ANOVA um ou dois fatores e as médias comparadas pelo teste de Tukey ($p<0,05$). A adição de PT reduziu o tempo de endurecimento dos materiais testados. Após 24 horas os cimentos 40/0 e 35/5 apresentaram maior solubilidade que os demais e após 14 e 28 dias o cimento 20/20 foi o que apresentou menor solubilidade ($p<0,05$). Após 7 dias o grupo 20/20 estabilizou a sua solubilidade. O cimento 40/0 apresentou os maiores valores e o cimento 20/20 apresentou os menores valores de resistência à tração diametral e módulo de elasticidade ($p<0,05$). A adição de PT a cimentos à base de cálcio possibilita benefícios ao tempo de presa e solubilidade.

Acknowledgements

The authors would like to thank Angelus for supplying the materials (MTA) of this study.

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Received April 16, 2017
Accepted October 10, 2017