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Single-cone obturation in endodontics: GuttaFlow vs Bioceramic sealers.

A systematic review.

Marine Emmeline Genevieve Vautier

Dissertação conducente ao Grau de Mestre em Medicina Dentária (Ciclo Integrado)

Gandra, 07 maio de 2022

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Trabalho realizado sob a Orientação de Prof. Doutor Pedro Jorge Bernardino.

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Aos meus pais, ao que me ensinaram, tudo o que representam, ao apoio infalível e pela incrível vida que me deram.

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RESUMO

Objetivo: O objetivo deste estudo foi realizar uma revisão integrativa comparando o sucesso clínico dos cimentos de obturação Guttafllow e Bioceramicos em termos de adaptação marginal às paredes dentinárias e biocompatibilidade usando a técnica de obturação de cone único.

Materiais e Método: Foi realizada uma pesquisa bibliográfica na base de dados PubMed usando os seguintes termos científicos: "adaptação marginal" OR "biocompatibilidade" AND "selantes biocerâmicos" OR "Endosequence BC" OR "Ceraseal" OR "TotalFill BC" OR "iRoot SP " OR "GuttaFlow" AND "tratamento endodôntico" OR "obturação de cone único". Os estudos publicados em Inglês, Francês, Espanhol e Português de janeiro de 2005 a setembro de 2021 foram selecionados com base no objetivo deste estudo.

Resultados: Relacionando a capacidade de selamento, os resultados anteriores relataram que GF e EndoSequence BC têm uma excelente capacidade de preenchimento e adaptação marginal às paredes dentinárias parecendo superiores ao CeraSeal, TotalFill BC e iRoot SP que não apresentam selamento significativamente melhor. Em termos de biocompatibilidade, os resultados de todos os biocerâmicos mostram um forte potencial bioativo e aumento da citocompatibilidade. Quanto ao GF, também é biocompatível, mas tem efeitos biológicos menos benéficos.

Conclusões: Em relação à adaptação marginal e biocompatibilidade do GF e dos biocerâmicos, ambos apresentam excelentes capacidades e não são significativamente diferentes. No entanto, os biocerâmicos tendem a ser mais adequados para o uso da técnica de obturação de cone único devido à sua forte biocompatibilidade.

PALAVRAS-CHAVE: "tratamento endodônticos", "cimentos biocerâmicos", "GuttaFlow", "obturação de cone único", "biocompatibilidade", “adaptação marginal”.

ABSTRACT

Purpose: The purpose of this study was to perform an integrative review comparing the clinical success of Guttafllow and Bioceramic sealers in terms of marginal adaptation to dentin walls and biocompatibility using the single-cone obturation technique.

Materials and Method: A bibliographic review was performed in the PubMed database using the following scientific terms: "marginal adaptation" OR "Biocompatibility" AND "bioceramic sealers" OR "EndoSequence BC" OR "CeraSeal" OR "TotalFill BC" OR "iRoot SP" OR "GuttaFlow" AND "Endodontic treatment" OR "single-cone obturation". Studies published in English, French, Spanish and Portuguese from January 2005 to September 2021 were selected based on the purpose of this study.

Results: Regarding the quality of the sealing ability, the previous findings reported that GF and EndoSequence BC have an excellent filling capacity and marginal adaptation to the dentinal walls appearing superior to CeraSeal, TotalFill BC and iRoots SP which do not show significantly better sealing. In terms of biocompatibility, the results of all bioceramics show a better bioactive potential and increased cytocompatibility. As for GF, it is also biocompatible but has less beneficial biological effects.

Conclusions: Regarding marginal adaptation and biocompatibility of GF and bioceramics, both show excellent capabilities and are not significantly different. However, bioceramics tend to be more suitable for the use of the single-cone obturation technique due to their strong biocompatibility.

KEYWORDS: "endodontic treatment", "bioceramic sealers", "GuttaFlow", "single-cone obturation", "biocompatibility", “marginal adaptation”.

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List of acronyms and abbreviations

MTA Fillapex – Mineral Trioxide Aggregate-based Fillapex

LP – Periodontal ligament

GF – GuttaFlow

GF Bioseal – GuttaFlow Bioseal

GF2 – GuttaFlow 2

BC – Bioceramic

SEM – Scanning electron microscopy

CS – CeraSeal

hPDLSC – Human periodontal ligament stem cells

1. INTRODUCTION

The purpose of root canal endodontic treatment is to eliminate the microorganisms infecting the root canal systems, to disinfect it and then to close it with sealing cements and gutta percha. This preparation of the canal is a key step for the success of this treatment. As for the obturation, it will then allow the canal to be hermetically and three-dimensionally closed, thus avoiding its bacterial re-infection, which is a crucial step because more than 60% of root canal treatment failures are due to a bad filling leaving spaces in the treated root canal[1,2].

The cold lateral compaction technique in combination with an endodontic sealer is an obturation technique often used as a reference. However, this standard approach does not provide a fluid-tight seal of the root canal system, for reasons such as lack of adaptation of the gutta-percha with the walls of the root canal, inability to bridge irregularities in the canal, a lack of uniform density of the filling material as well as its resorption over time. This technique also remains operator-dependent and the resulting compaction forces can cause damage to the dentin such as dentinal debris, cracks and vertical root fractures[3,4].

An alternative to this technique is the single-cone obturation technique which uses a single, more conical gutta-percha cone with dimensions matching those of the last instrument used during root canal preparation. The main advantage of this technique is to ensure that a large volume of gutta-percha will be placed in the canal in a short time. Similarly, the use of a cone of the size corresponding to the root canal offers a satisfactory obturation of the latter in terms of shape, length and homogeneity, mainly in the apical third. Moreover, this technique involving no accessory cones and compaction can be considered as a less damaging method for the dentinal wall[3-6].

When the single-cone obturation technique is used, a sealer with adequate physical and chemical properties is relied upon as this plays a major role in producing a bond between gutta-percha and dentin. Several commercially available sealers with different adhesive mechanisms have been designed aimed at filling irregularities between the cone and dentin walls, accessory canals, and

sealing the dentinal tubules to prevent root canal infection. An ideal sealer must meet several criteria: it must be biocompatible, adapt to the dentinal walls ensuring good adhesion during setting without undergoing dimensional deformations and must form a tight apical seal. In addition, it must be bacteriostatic and form a bond between the core of the filling material and the wall of the root canal by burying the remaining bacteria. Finally, a sealer should be insoluble in tissue fluids but soluble in common solvents if it is necessary to remove the root canal filling[5-8].

Two types of sealing cements have recently been introduced using the single-cone obturation technique: those based on silicone and those based on bioceramics.

GuttaFlow, a new silicone-based sealer, is a cold, fluid filler system that flows easily into dentinal canals and tubules, providing maximum seal quality[9].

This contains a mixture of gutta-percha and polydimethylsiloxane powder with nanoscale silver particles added as a preservative. GuttaFlow2, an evolution of GuttaFlow, is a system combining gutta-percha powder with a grain size of less than 30 mm and a sealant. These two sealers differ in the shape of the silver particles used[9-12].

A new formulation of polydimethylsiloxane with gutta-percha powder combined with calcium silicate particles using the same system has been introduced and named GuttaFlow Bioseal[11-14]. It contains bioactive substances such as calcium and silicate, which stimulates tissue regeneration thanks to its power to form hydroxyapatite[10, 12]. Its working and hardening time is shorter than that of GuttaFlow 2[13, 14].

Bioceramic-based endodontic sealers have only been available for thirty years[15]. They are composed of alumina, zirconia, bioactive glass, glass ceramic, hydroxyapatite and calcium phosphates. The classification of bioceramic materials into bioactive or bioinert materials depends on their interaction with the surrounding living tissues. Bioactive materials, such as glass and calcium phosphate, interact with surrounding tissues to promote the growth of longer-lasting tissues[14, 16, 17].

Bioceramics are ceramic compounds with excellent biocompatibility properties due to their hydration process producing different compounds such as

hydroxyapatites, having the ability to induce a regenerative response in the human body[8, 14, 16, 17].

Bioceramic sealers also have the quality of providing antibacterial properties. They form porous powders containing nanocrystals with a diameter of 1 to 3 nm, which prevent bacterial adhesion[8].

The calcium silicate sealer has calcium releasing ability, adequate biocompatibility, and similar sealing properties and ability to conventional sealers such as AH Plus. Recently, many products with a sealer based on calcium silicate in a syringe have been developed. These products have the advantage of being easily applied to the root canal, absorbing moisture from the dentinal tubule and eliminating the mixing process since the calcium silicate sealer sets on its own. Calcium silicate sealers form calcium hydroxide, hydroxyapatite and a mineral infiltration layer on the dentin wall, which improves the bonding ability with dentin. In addition, these sealers produce a mechanical fit to a dentinal wall by diffusing into the dentinal tubules[18-22].

In this study, Endosequence BC™ Sealer® (Brasseler USA, Savannah, GA, USA), CeraSeal™ Sealer® (Meta Biomed, Cheongju, Korea), TotalFill BC™ Sealer® (FKG Dentaire SA, La-Chaux-de-fonds, Switzerland) and iRoot SP™ Sealer® (Innovative BioCreamix Inc., Vancouver, Canada) will be the examples of bioceramics sealers chosen. They are ready-to-use premixed injectable materials composed of calcium phosphate, calcium silicates, monobasic calcium phosphate, calcium hydroxide, zirconium oxide, fillers and thickening agents, which require the presence of water to harden. It does not shrink when setting and has excellent physical and biological properties[23, 24, 25].

2. Objectives and Hypotheses

The aim of this study is to compare the clinical success of Guttaflow and Bioceramic sealers in terms of marginal adaptation to dentinal walls and in terms of biocompatibility through the single-cone obturation technique.

In relation to this objective, this comparison will verify the hypothesis that there is one sealer with better marginal adaptation and biocompatibility than the other.

3. MATERIALS AND METHODS

3.1. Protocol and registration

This systematic review was conducted according to the PRISMA statement (Preferred Reporting Items for Systematic Reviews), and the protocol was registered in the International Prospective Register of Systematic Reviews, PROSPERO.

3.2. Eligibility Criteria

The 'PICOS' approach was used independently, and the search strategy was discussed between with three other investigators to extract data from the selected articles. PICOS stands for "population (participants), intervention (or exposure for observational studies), comparator, outcomes and study design" (*Table 1*).

Population :	Extrated mature permanent human teeth.
Intervention :	Single-cone obturation technique in endodontic.
Comparison :	Treatment using GuttaFlow or Bioceramic sealers.
Outcomes :	Clinical efficiency, biocompatibility, marginal adaptation, sealing ability.
Study design :	Clinical trial, comparative study, randomized controlled.

Table 1- PICOS considerations

The eligibility criteria used for article searches are as followed *(Table 2)*:

Insertion criteria	*Exclusion criteria*
- Articles published between 2005 and 2021. - Articles published in English, French, Spanish and Portuguese. - Studies with human permanent mature teeth. - Clinical trial, comparative study, randomized controlled, systematic review. - Single-cone technique. - GuttaFlow and Bioceramic sealers.	- Abstracts missing. - Theses, dissertations, Letters to the editor. - Others sealers. - Repair sealers. - Immature teeth. - Others treatment endodontics with several cones obturation technique. - Incomplete and poorly data accessibility.

Table 2- Eligibility criteria

3.3. Information sources:

A systematic search was performed in English, French, Spanish and Portuguese published between January 2005 and September 2021 on the PubMed (via the National Library of Medecine) databases. The research used keywords and MeSH terms related to the topic in question.

3.4. Search Strategy:

Data Base	Research Equation	Identified Articles	Selected articles
PubMed	1:((ceraseal) AND (endodontics (MeSH Terms)) 2: :((clinical trial) OR (comparative study) OR (randomized controlled)) 3 :1 AND 2	4	4
	1:((endosequence bc sealer) AND (endodontics (MeSH Terms)) 2:((clinical trial) OR (comparative study) OR (randomized controlled)) 3 :1 AND 2	37	5
	1:((totalfill) AND (endodontics (MeSH Terms)) 2:((clinical trial) OR (comparative study) OR (randomized controlled)) 3 :1 AND 2	56	5
	1:((iroot sp sealer) AND (endodontics (MeSH Terms)) 2:((clinical trial) OR (comparative study) OR (randomized controlled)) 3 :1 AND 2	56	4

	1:((bioceramic sealers) AND (endodontics (MeSH Terms)) 2:((clinical trial) OR (comparative study) OR (randomized controlled)) 3 :1 AND 2	52	6
	1:((single-cone obturation) AND (endodontics (MeSH Terms)) 2:((clinical trial) OR (comparative study) OR (randomized controlled)) 3 :1 AND 2	95	9
	1:((guttaflow) AND (endodontics (MeSH Terms)) 2:((clinical trial) OR (comparative study) OR (randomized controlled)) 3 :1 AND 2	52	8

Table 3- Detailed search strategies

3.5. Study selection:

Stage I: Preliminary review of the abstracts, accessible studies, titles were performed to determine if the articles met the intended purpose for the study.
Stage II: Quality assessment was performed on the studies that fulfilled the inclusion criteria. The quality and design of the study was considered.
Stage III: A thorough evaluation was completed. Summaries of the included articles were prepared and information regarding study design, subjects, treatment time, and outcomes were organized in tabulated form.

4. RESULTS

4.1. Study selection

Overall, after duplicates records removed, of the 193 studies reviewed (Stage I), 131 were excluded because they did not provide comprehensive data considering the purpose of the present study. 62 were selected for further review (Stage II). Of these 62 articles, 21 were rejected insofar as they did not include statistical data that could allow us to answer our question. Of the 41 full-text articles assessed for eligibility, 26 were excluded for our study. Ultimately, 15 studies were included in the systematic review (Stage III).

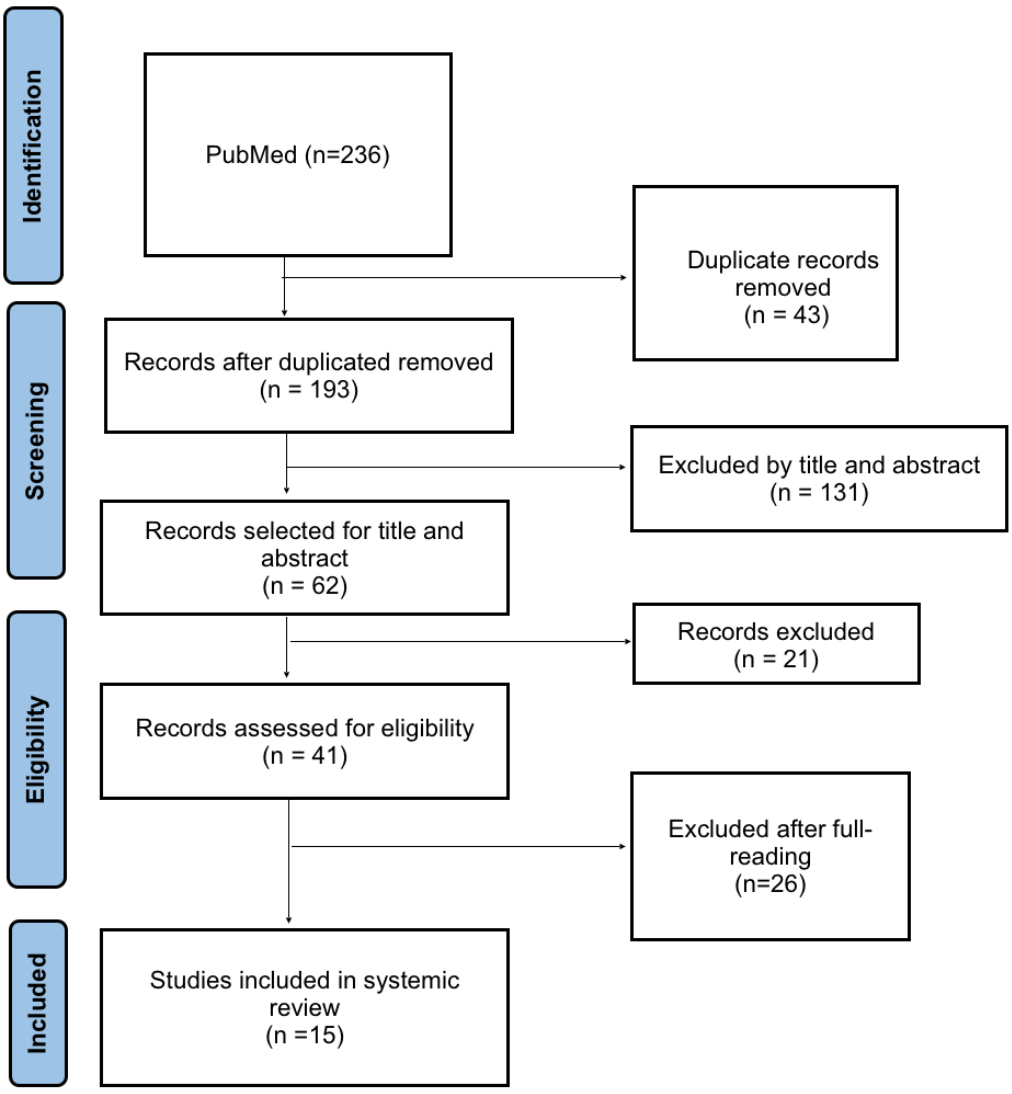

Diagram 1- PRISMA Flow diagram of the search strategy used in this study.

4.2. Data items and collection

The following information was determined from the articles: names of the authors and year of publication, purpose and methods, study design, results obtained. *(Table 4)*

Author/Year	Purpose/Methods	Study design	Results
Collado-Gonzálo, M et al. 2017	Evaluate the cytotoxicity of GF bioseal, GF2, MTA Fillapex and AH Plus LP stem cells.	Randomized in vitro study	Cell viability was evident after 24 hours with GF bioseal and GF2 but no with AH Plus and MTA Fillapex. The microscopy studies revealed a high degree of proliferation, cell spreading and attachment especially with GF Bioseal. Finally, the GF Bioseal and GF2 showed lower cytotoxicity than MTA Fillapex and AH Plus.
Rodríguez-Lozano, FJ et al. 2019	To evaluate and compare the biological effects and the cementogenic potential of different endodontic sealants in contact with human periodontal ligament stem cells (hPDLSCs): MTA Fillapex and the two new silicone-based sealants GuttaFlow2 and GuttaFlow Bioseal. AH Plus was used as a reference material.	Randomized in vitro study	More than 90% of the viable cells were obtained using extracts of GuttaFlow Bioseal and GuttaFlow2 after 72 hours of culture. In contrast, AH Plus and MTA Fillapex induced significantly lower levels of cell viability. GuttaFlow2 and GuttaFlow Bioseal promoted wound closure in a concentration dependent manner. With AH Plus and MTA Fillapex, cell migration was significantly lower. SEM analysis revealed a high degree of cell adhesion on the GuttaFlow Bioseal discs. These results showed that GuttaFlow sealers were more cytocompatible than AH Plus and MTA Fillapex, while GuttaFlow Bioseal favored cementoblast differentiation of hPDLSCs in the absence of any growth factors.

Wu, D et al. 2011	Evaluate the sealing ability of GF with a study using the percentage of gutta percha filled area in 80 mandibular first premolars with single canal were randomly divided into 4 groups(n=20) according to root canal filling technique and/or material.	Randomized in vitro study	Group3 (GF) and group4 (GF and accessory gutta percha without lateral condensation) have significantly higher than group1 (cold lateral condensation technique) and group2 (continuous wave condensation technique). Finally, GF provided superior sealing ability, such that accessory gutta percha cones became unnecessary when filling root canals with GF.
Zhou, H et al. 2013	Evaluate the PH change, viscosity, solubility and film thiknesses of MTA Fillapex, Endosequence BC, GF, AH Plus and Pulp canal sealer during periods of 1 day and 5 weeks.	Comparative study	The MTA Fillapex and Endosequence BC sealers each possessed comparable flow and dimensional stability but higher film thickness and solubility than the other sealers tested.
Chybowski, E et al. 2018	Evaluate the outcome of nonsurgical root canal treatment using a single-cone and Endosequence BC technique and to identify factors associated with success or failure on 307 teeth with a minimum of a 1 year recall after treatment. Teeth were classified as healed, healing (success), or not healed (failure).	Comparative study	The overwall success rate was 90,9%. Lesions <5mm in diameter had a significantly higher success rate than lesions >5mm. Sealer extrusion was observed in 47,7% of the cases. The presence of sealer extrusion did not have any significant effect on the treatment outcome. Endosequence BC used with a single-cone technique is a viable option for obturation.
Zhong,X et al. 2019	Compare the quality of root fillings completed by single-cone obturation technique with 3 different sealers (GF bioseal, GF2 and MTA Fillapex) after minimal instrumentation and multisonic cleaning of root canals of 18 maxillary first molars.	Comparative study	The 3 groups had 90%-99% of the canal space filled with the root filling material. The mean volume of the filling material was higher in the GF Bioseal and GF2 groups than in the MTA Fillapex group ($P < .05$). There was no significant difference among the apical, middle, and coronal thirds.The cross-sectional images showed no obvious gaps or voids in the GF groups. After instrumentation, 49 of the 189 canal thirds (25.9%) had hard tissue debris in the root canal system. After GentleWave cleaning, only 4 of 63 canals (6.3%) and 4 of the 189 canal thirds (2.1%) still had debris. The single-cone obturation method with GF2 and

			GF Bioseal sealers after multisonic cleaning of minimally instrumented molar canals resulted in high-quality root fillings.
Nigri Roizenblit, R et al. 2020	Compare, by micro-computed tomography analysis, the obturation quality of two filing methods: the single-cone technique with the bioceramic Endosequence BC and the continuous technique with the AH Plus sealer with 20 mandibular molars were divided into 2 groups (n=10) according to the sealer used and were only the mesial roots was used.	Comparative study	There was no significant difference between groups for filling volume, voids and gaps. Using two filling methods, Endosequence BC and AH Plus promoted a similar root filing quality in mesial roots of mandibular molars.
Mestieri, LB et al. 2019	Evaluate the cell viability and migration of Endosequence BC sealer compared to MTA Fillapex and AH Plus who were placed in contact with culture medium to obtain sealers extracts in 3 different dilution and after 3T3 cells were plated and exposed to those extracts.	Comparative study	This study revealed greater cytotoxicity for AH Plus and MTA Fillapex than Endoscequence BC. Moreover, at 36hours, only Endosequence BC presented the closure when compared to others sealers. All tested sealers demonstrated cell viability highlighting Endosequence BC Sealer, which showed increased cell migration capacity suggesting that this sealer may achieve better tissue repair when compared to other tested sealers.
Asawaworarit, W et al. 2020	Evaluate the apical sealing ability of bioceramic (EndoSequence BC) and epoxy resin-based (AH Plus) sealers at 24 h, 7 days and 4 weeks in 42 extracted human upper anterior teeth were sectioned to leave the root 15-mm long, then all the roots were instrumented using a set of ProTaper rotary instruments. In this study, 4 roots were selected randomly as controls, and the remaining 38 roots were randomly divided in 19 roots each: group1: EndoSequence BC, and group 2: AH Plus.	Comparative study	Using fluid filtration method, the present study found EndoSequence BC had significantly better apical sealing ability than AH Plus at 24 h, 7 days, and 4 weeks ($P < 0.001$). The results of SEM evaluation showed EndoSequence BC has better adaptation and higher sealer penetration into the dentinal tubules than AH Plus, especially in the apical third of root canals.

	The apical sealing ability of the filled root canal was measured using the fluid filtration method with 200 mmHg (26.67 KPa) above atmospheric pressure at 24 h, 7 days and 4 weeks. Scanning electron microscopy (SEM) was used to assess the adaptation and penetration of the sealers. The apical microleakage between 2 groups was compared using Student's t-test. $P < 0.05$ was considered statistically significant.		
López-García, S et al. 2020	Evaluate the biological properties of CSBS: EndoSequence BC Sealer, Ceraseal, and Endoseal mineral trioxide aggregate in hPDLSCs. The ion release profile and pH were determined, and metabolic activity and cell migration were assessed using the MTT. hPDLSCs were cultured in direct contact with the surface of each material, and cell morphology and attachment were analyzed by SEM. Bioactivity potential was assessed by RT-qPCR and mineralization assays.	*Randomized in vitro study*	All materials showed an alkaline pH, although Endoseal exhibited a significantly higher pH compared with the other CSBS. Ceraseal released significantly more Ca^{2+} than EndoSequence BC Sealer and Endoseal. Interestingly, Endoseal induced a significant reduction in cell viability and cell migration compared with the control. Moreover, SEM showed abundant cells adhering to EndoSequence BC Sealer and Ceraseal surfaces, whereas very few round cells were detected on the surface of Endoseal. Finally, Ceraseal and EndoSequence induced ALP, CAP, and CEMP-1 expression and a significantly higher mineralization capacity than Endoseal. The eluates from EndoSequence BC Sealer and Ceraseal displayed higher cell viability, cell attachment, cell migration rates, and ion release rates than Endoseal. Ceraseal and EndoSequence BC Sealer exhibited significantly more gene expression and mineralization capacity than Endoseal.
Kharouf, N et al. 2020	Compare the physicochemical properties, filling ability, and antibacterial activity of a premixed calcium silicate-based sealer to those of a powder–liquid bioceramic sealer. Ceraseal (CS) and BioRoot (BR)	*Comparative study*	Statistically significant lower void percentages were observed for CS at 2 and 8 mm from the working length (WL) compared to those for the BR group, whilst no significant difference was observed at 5 mm from the WL. BR sealer showed higher alkaline pH, rougher surface,

	materials were analyzed using scanning electron microscopy and energy-dispersive X-ray spectroscopy at 7 and 14 d of immersion in distilled water. The filling ability of the two sealers as well as the water contact angle, solubility, flow, roughness, crystalline microstructure, pH, and compressive strength were also evaluated. The antibacterial activity was assessed through an agar diffusion as well as through direct tests.		lower water contact angle values, lower flowability, and higher solubility compared to CS. BR showed globular and needle-like crystalline microstructure, whilst CS had globular and flower-like crystalline microstructure up to 72 h. No statistical difference was found for the compressive strength between the two sealers. BR and CS showed no antibacterial effect against *Enterococcus faecalis* after 3 h, whilst both sealers showed antibacterial capacity after 24 and 72 h. BR demonstrated higher antibacterial activity after 24 h.
Oh, H et al. **2020**	Evaluate the biocompatibility of calcium silicate-based sealers (CeraSeal and EndoSeal TCS) and epoxy resin-based sealer (AH-Plus) in terms of cell viability, inflammatory response, expression of mesenchymal phenotype, osteogenic potential, cell attachment, and morphology, of hPDLSCs were acquired from the premolars (n = 4) of four subjects, whose ages extended from 16 to 24 years of age.	*Comparative study*	Flow cytometry analysis showed stemness of hPDLSCs was maintained in all materials. In cell viability test, AH-Plus showed the lowest cell viability, and CeraSeal showed significantly higher cell viability than others. In ELISA test, AH-Plus showed higher expression of IL-6 and IL-8 than calcium silicate-based sealers. In an osteogenic potential test, AH-Plus showed a lower expression level than other material; however, EndoSeal TCS showed a better expression level than others. All experiments were repeated at least three times per cell line. Scanning electronic microscopy studies showed low degree of cell proliferation on AH-Plus, and high degree of cell proliferation on calcium silicate-based sealers.
López-García, S et al. **2019**	Investigate the cytocompatibility and mineralization potential of two premixed hydraulic endodontic sealers compared with an epoxy resin-based root canal sealer. The cellular responses and mineralization capacity were studied in hPDLSCs that were exposed to premixed hydraulic sealers, Bio-C Sealer, TotalFill BC Sealer and an epoxy resin-based material, AH Plus. Non-exposed cultures served as the	*Randomized in vitro study*	AH Plus reduced cell viability and cell migration, whereas increased cell viability and cell migration were observed in the Bio-C Sealer and the TotalFill BC Sealer. The lowest cell attachment and spreading were observed for all concentrations of AH Plus, whereas the highest were observed for TotalFill BC Sealer. At the end of 21 days, only the Bio-C Sealer and the TotalFill BC Sealer supported matrix mineralizatio. Additionally, SEM-EDX revealed

	control. The endodontic sealers were assessed using SEM and energy dispersive X-ray microanalysis (EDX).		high content of calcium, oxygen, and silicon in the Bio-C Sealer and the TotalFill BC Sealer.
Rodríguez-Lozano, FJ et al. **2017**	Investigate in vitro the cytocompatibility of the calcium silicate-containing endodontic sealers MTA Fillapex and TotalFill BC Sealer on hPDLSCs by assaying their biological responses and compare them with that observed when using AH Plus. Specimens from the three different endodontic sealers were eluated with culture medium for 24 h. The cytotoxicity of these eluates was evaluated using the MTT assay. In addition, an in vitro scratch wound healing model was used to determine their effects on cell migration. Cell adhesion to collagen type I after treatment with the different sealer eluates was also measured, whereas cytotoxicity was determined using the DNA-specific fluorochrome Hoechst 33342. Finally, to assess cell morphology and attachment to the different sealers, hPDLSCs were directly seeded onto the material surfaces and analysed by SEM.	*Randomized in vitro study*	hPDLSCs exposed to different dilutions of TotalFill BC Sealer eluates had significantly higher cell proliferation compared with that observed when cells were treated with AH Plus and MTA Fillapex eluates. In addition, TotalFill eluates were associated with significantly increased cell adhesion to collagen type I and migration of hPDLSCs in a concentration-dependent manner than displayed after treatment with MTA Fillapex or AH Plus eluates. Moreover, TotalFill BC Sealer-induced cytotoxicity was significantly lower than observed using AH Plus and MTA Fillapex eluates. Finally, SEM studies revealed suitable proliferation, cell spreading and attachment, especially when using TotalFill BC Sealer discs. TotalFill BC Sealer exhibited a higher cytocompatibility than AH Plus and MTA Fillapex. Further investigations using in vivo animal models are required to validate the potential biological responses of TotalFill BC Sealer on hPDLSCs.
Gandhi, B et al. **2017**	Evaluate and compare the apical sealing ability of two endodontic root-end filling materials namely, iRoot SP and ProRoot MTA using the bacterial leakage system. A total of fifty recently extracted, single rooted teeth with a single straight canal were selected for the study. The teeth were chemo mechanically prepared. The apical 3mm of the root was resected and root end cavities were prepared. The teeth were randomly divided into two groups	*Comparative study*	The ProRoot MTA filled root end samples leaked within 30-72 days. The iRoot SP filled root end samples leaked within 51-69 days. All the tested materials showed significant apical sealing ability as root-end filling materials over a period of 90 days. iRoot SP exhibited the most effective apical sealing ability as compared to ProRoot MTA.

	of twenty teeth each for the experimental root end filling materials namely, iRoot SP and ProRoot MTA. Leakage was assessed for 90 days and compared using survival statistics.		

Table 4- Relevant data collected from selected studies.

5. DISCUSSION

This integrative review aims to highlight new innovative sealing cements such as GuttaFlow and bioceramic sealers through a new endodontic obturation treatment technique using a single-cone. However, for the results to be conclusive, each step of the root canal preparation must first be observed. In fact, the root canal must be prepared as best as possible by removing the infectious media as much as possible, limiting the remains of bacteria and root remains before filling and this by providing perfect irrigation throughout the preparation. Also, the type of instrumentation is also taken into account, whether manual or rotary and including the quality of the operator's handling. The use of a certain type of gutta percha can also influence the success of the treatment because it must adapt to the type of root canal being treated (complex, curved)[1,2,7].

Historically, root canal treatment failure has been associated with poor root canal filling. These results suggest the importance of obturation techniques and materials[26].

The single-cone obturation technique has shown that it allows to have a large volume of gutta percha within the canal system, thus allowing good adaptability to the conicity of the canal. This adaptability makes it possible to limit damage to the dentinal walls and also makes it possible to reduce empty spaces and porosity and thus limit bacterial infiltration by forming a good seal. This technique also allows good fluid and three-dimensional filling of the sealer into the root canal system. In short, the single-cone obturation technique allows a more efficient and faster treatment than the others. However, studies conducted on this technique do not confirm that it is effective for all types of canals[7].

GuttaFlow is an innovative sealing cement that is used through the unique cone sealing technique. In the studies carried out it is often differentiated into two groups according to its composition: GuttaFlow Bioseal and GuttaFlow2. As GuttaFlow2 does not have bioactive particles in its components, studies are mainly focused on GuttaFlow Bioseal which contains it.

As for the studies carried out on the biological properties of GuttaFlow, cytotoxicity tests are primary biocompatibility tests that determine cell activity, inhibition of growth, cell lysis and other effects on them caused by the substances tested. In vitro cytotoxicity studies are essential to assess the safety of endodontic cements and their chemical-biological interactions, in order to ensure the viability of periradicular cells and the absence of cell death pathways such as apoptosis. or necrosis[10].

Collado-Gonzálo, M et al.[12] conducted a study on the cytotoxicity of GuttaFlow Bioseal, GuttaFlow2 in comparison with other sealers. This study showed that after 24 hours the cells of the periodontal ligament were significantly more viable than for other cements. GuttaFlow in general is a very low toxicity cement, certainly due to the fact that it is composed of bioactive components and hydroxyapatite particles, which then allow hydration of these cells to be created.

It was *Rodríguez-Lozano, FJ et al.*[14] who conducted a study showing the cementogenic effects of GuttaFlow2 and bioseal in comparison with other sealers. In addition to hydrating the cells of the periodontal ligament, GuttaFlow allows them to differentiate and migrate. This cell viability is also due to the strong biocompatibility and adaptability of GuttaFlow in general with the dentinal walls.

Indeed, the marginal adaptability to the dentinal walls is visible by the ability of GuttaFlow to fill a root canal and leave very little empty space within the root canal system because according to the study by *Zhong, X et al*.[27] GuttaFlow has a 90% -99% channel filling capacity. Therefore, the so little empty space left by this sealing cement suggests that it provides excellent microbial sealing.

The in vitro study by *Wu, D et al.*[9] aims to use a method that examines high magnification micrographs of cross sections of the root canal coupled with image analysis to assess the sealing ability of GuttaFlow. Depending on the results obtained, GuttaFlow allows a tight seal, leaving no microbial leakage. Finally, according to him, GuttaFlow does not undergo shrinkage but a slight expansion of 0.2% and it retains elasticity even after hardening. GuttaFlow then appears to be an excellent sealer in the single-cone obturation technique, both in terms of its adaptability and its biocompatibility.

Among the new generations of bioceramic sealers, Endosequence BC Sealer is a new bioceramic sealer based on phosphate and calcium silicate, calcium hydroxide, zirconium oxide, filler and thickening agents.

Endosequence BC demonstrates many properties such as biocompatibility, chemical stability, hydrophilicity, fluidity, radiopacity and marginal adaptability to tooth walls. This sealer has also been shown to have an antimicrobial effect on bacteria known to be resistant to disinfection procedures such as Enterococcus faecalis[24, 25].

In addition, the superior fluidity and the ability to expand slightly upon setting allows this sealer to be used in a single cone obturation technique. The sealer sets on contact with moisture, mainly from the dentinal tubules. Thus, these qualities of the Endosequence BC have improved the efficiency of root canal filling and may provide better sealing in otherwise inaccessible root canal anatomies[24].

Additionally, *Asawaworarit, W et al.*[28] demonstrated in their study that Endosequence BC has ideal sealing ability. Indeed, by using the fluid filtration method and the SEM evaluation, it would have a better adaptation and a greater penetration of the sealer into the dentinal tubules as well as a significantly better apical sealing capacity than the other sealing cements used in comparison especially in the apical third of the root canals. This adaptation and tightness can be explained by both physical and chemical phenomena. Indeed, due to the size of the particles of the Endosequence BC which are smaller (0.2mm) allowing to improve the penetration of these in the dentinal tubules in particular at the apical level of the root and thus to improve the retention mechanics of the sealer on the dentin walls forming a physical barrier to prevent microleakage from the root canal system. EndoSequence BC also has a hydrophilic property which thanks to the moisture remaining in the dentinal tubules triggers its setting reaction with the production of hydroxyapatite, thus creating the chemical bond with the root dentin. This chemical bond could improve the adaptation to the root canal wall and help prevent microleakage[8, 28].

Chybowski, E et al.[24] evaluated the success rate of endodontic treatments and the appearance of sealer extrusion on lesions (> 5mm or <5mm) using the single-cone obturation technique with Endosequence BC as sealing cement and

stated that this technique is a viable option for obturation as the success rate was 90.9% and extrusion was insignificant.

This is also confirmed by the study carried out by *Nigri Roizenblit, R et al.*[25] demonstrating the filling quality of the Endosquence BC sealer.

This filling and flow quality allowing a good seal has also been the subject of a study by *Zhou, H et al.*[23] and *Al-Haddad, A et al.*[26] who both compared the physical properties of Endosequence BC to other sealers and assert from their results that it has very good flow and dimensional stability and with a higher film thickness and solubility than other sealers tested (GuttaFLow, AH Plus, MTA Fillapex). These physical qualities make Endosequence BC a very good antimicrobial sealer. But it also has very good biological qualities.

Indeed, bioceramics produce, during the hydration process, different compounds, (ex. Hydroxyapatites), with the ability to induce a regenerative response in the human body. When placed in contact with bone, the mineral hydroxyapatite has an osteoconductive effect, leading to bone formation at the interface[8]. The Endosequence BC is also known for its biocompatibility and bioactivity. *Boldrin Mestieri, L et al.*[29] tested different sealers (Endosequence BC, MTA Filapex, AH Plus) and they demonstrated cell viability highlighting the Endosequence BC Sealer and its biocompatibility because it showed a capacity for cell migration increased, suggesting that this sealer may achieve better tissue repair compared to other sealers tested. This capacity is also supported by *Giacomino, CM et al.*[30] carrying out a study on the bioactive and osteogenic capacity of Endosequence BC and following these results demonstrates that bioceramic cementitious materials such as Endosequence BC sealer have a lasting bioactivity through the diffusion of molecules during and after their setting. This new generation of bioceramic sealers like Endosequence BC has desirable characteristics while being able to modulate the apical tissue environment.

As for Ceraseal, this too is a recently launched premixed endodontic sealer containing calcium aluminates, zirconium oxides and thickening agents. The synthesized pure calcium silicate compound was used for CS. In addition, despite the lack of studies carried out, it still appears that CS has good conditions for its use in endodontics. Indeed, it has good biocompatibility due to its high potential

for bioactivity given its composition. This bioactivity is very important for the correct formation of hard mineral tissue and involves the synthesis of calcium phosphate deposits on the surface of the material placed in a mimetic body fluid[18-20].

Lopez-García, S et al.[18] reported that CS released a high amount of Ca2+ ion, confirming its bioactive capacity and leading to promote tissue healing. This healing would also be due to a capacity for adhesion and significant cell viability. Moreover, when in direct contact with cell types more closely associated with a clinical situation such as hPDLSCs, CS reacts by inducing some mineralization as well as the gene expression of CEMP-1, linked to the formation of cementum and osteoblastic differentiation. The study by *Oh, H et al.*[19] supporting these same properties, makes it possible to affirm that CS is a bioceramic which presents a certain biocompatibility[19].

Regarding the physical properties of CS, here too few studies have been conducted. However, CS was the subject of a study by *Kharouf, N et al.*[21] aiming to show that it would also have a good marginal adaptation to the dentinal walls thanks to its quality of filling. Indeed, these authors carried out flow and solubility tests and evaluated the void percentages of the interfacial spaces in the apical, medial and coronal parts of the root canal. The results of these studies made it possible to show that the CS presented a significant fluidity allowing a good penetration in the dentinal tubules. This fluidity may be the reason for a high rate of solubility obtained as well as the observation of a low percentage of void thus inducing an adequate filling capacity. Thus, CS appears to be a suitable bioceramic sealer for endodotic treatments but these results still need to be confirmed by more studies because it still appears that it shows low dimensional stability over time according to *Park, MG et al.*[20]

Just like CS, TotalFill BC Sealer is another bioceramic calcium silicate based sealer that has shown good physical and biological properties and has the ability to release calcium ions[22, 31, 32]. However, as TotalFill BC is also a recently developed bioceramic sealer few studies have been conducted on these properties. Nevertheless, *López-García, S et al.*[22] as well as *Rodríguez-Lozano, FJ et al.*[31] have carried out studies on its biocompatibility. Indeed, both conducted

their studies using cultures of human periodontal ligament stem cells in the presence of extracts of TotalFill BC and other types of sealers. These studies assessed cytotoxicity, mineralization potential and cell proliferation using tests such as: immunofluorescence, SEM as well as the alizarin red assay to assess osteogenic potential. The results of these various tests were able to reveal a certain cell viability. Indeed, TotalFill BC presented highly adherent, proliferating and migrating cells on the surface of hPDLSCs and allowed a release of Ca2+ ions thus promoting differentiation and cellular mineralization. Taken together, TotalFill BC demonstrated better cytocompatibility in terms of cell viability, migration, cell morphology, cell attachment and mineralization capacity than the other sealers compared in these studies. It then appears that the composition of TotalFill BC plays an important role in its biological properties[22, 31, 32].

Although these results are promising, further investigations are needed regarding the marginal adaptation of this example of bioceramics sealers.

Finally, iRoot SP is an injectable, pre-mixed, radiopaque, insoluble, aluminum-free bioceramic sealer that is composed of calcium phosphate, calcium silicates, zirconium oxide, calcium hydroxide and mainly calcium silicates which can generate calcium silicate hydrates in the presence of water just like those predecessors included in this review[33-36].

This requires moisture from the dentinal tubules or periapical tissues to set and harden and comprises a composition similar to white mineral trioxide aggregate (MTA) material thus possessing both excellent physical and biocompatibility. Newly developed calcium silicate based MTA materials such as iRoot SP can be used as alternatives to MTA as apical plug materials for induction of hard tissue deposition due to their similar chemical components while remaining a sealant, not a repair. iRoot SP is also a calcium silicate cement, so it has good biocompatibility. It indeed allows a certain differentiation and cellular proliferation due to its compatibility which results in the promotion of periapical healing. In addition, some studies that have done solubility tests show that it has an increased porosity in its internal surface allowing the penetration of water over time and a high level of release of Ca2+ ions, which gives it a bioactive capacity. as seen previously[33,34].

As for its sealing ability, again few studies have been conducted. However, according to *Gandhi, B et a*l.[35], iRoot SP was found to be a suitable material for use as a root-tip filler. Indeed, using the bacterial leak system, the apical sealing capacity could be evaluated. Since iRoot SP does not shrink during setting and hardens in the presence of water, it would form an airtight seal inside the root canal at the apical level with or without the use of gutta-percha to form a monobloc. Similar results were observed by *Zhang, W et al.*[36]. Nevertheless, during these studies, iRoot SP did not show significant differences compared to other sealers and its adaptability was only studied at the apical level. Therefore, iRoot SP would therefore present a good biocompatibility but given the few studies on its physical properties, it remains difficult to assess its marginal adaptation to the dentin walls.

6. LIMITS

In this systematic review there are some limitations. First in the choice of inclusion criteria limiting languages, the studies focused only on humans and on extracted mature permanent teeth. Then for the methodology, the fact of using PubMed as a database to limit my research because studies were therefore excluded, and many articles could not be downloaded in pdf.

Regarding this study on the effectiveness of the single obturation cone technique in endodontic obturation treatments and the new sealing cements used therein, it is noted that there are certain limitations. Indeed, these have been set up recently and there are therefore still few studies carried out on their subject. Also, regarding bioceramic sealers, it was difficult to discern the differences between the existing types because many articles referred to repair bioceramics which is only used to repair dentinal canals and MTAFilapex but this one does not was not unanimous on its true definition, so they were excluded from the search, which narrowed the results. In addition, given that the examples taken to illustrate bioceramic materials are recent, few studies have been carried out, not to mention that most were not available in free pdf and therefore greatly reduced my research. In short, studies should be more in-depth and made on broader criteria to allow an adequate comparison of these materials. To fully confirm the effectiveness of the single-cone obturation technique and these sealing cements, studies should include other factors that may influence the success of its treatments such as the quality of the preparation of the root canal system, the choice of type of irrigation used as well as choice of gutta percha and type of instrumentation. As for the operator, the manner will always also influence the unveiling of the studies.

7. CONCLUSION

Considering the various articles carried out in this systematic review, we have been able to observe that the single-cone technique allows sealing in a shorter working time, less damaging and also allows the volume of the canal system to be optimized. It's possible and thus form a better seal than other techniques such as cold lateral compaction.

However, its sealing ability largely depends on the choice of sealing cement. The latter must be chosen, among other things, according to its marginal capacity to adapt to the dentinal walls and its biocompatibility, which represent the key points for the clinical success of an endodontic treatment.

In this study conducted on the properties of GuttaFlow and bioceramic cements, both have been shown to have satisfactory biocompatibility and sealing ability.

Nevertheless, studies are generally in favor of bioceramic sealers, due to their dimensional stability, their moisturizing and osteogenic power, as well as their great adaptability to the dentinal walls, in particular in the apical third of the roots. They seem to be ideal in case of root perforations, large apical foramen and root resorptions. This may therefore make it possible to respond to the initial hypothesis that there would therefore be a more effective sealer with the single-cone obturation technique, even if there are currently not many products available for endodontic use. As more products come to market and more research is done on these materials, this can provide more reliable data on clinical outcomes.

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