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Review article

Zirconia-reinforced lithium silicate (ZLS) mechanical and biological properties: A literature review

Fernando Zarone [a], Gennaro Ruggiero [a,*], Renato Leone [a], Lorenzo Breschi [b], Stefania Leuci [c], Roberto Sorrentino [a]

[a] Department of Neurosciences, Reproductive and Odontostomatological Sciences, Division of Prosthodontics and Digital Dentistry, University "Federico II" of Naples, Via Pansini 5, 80131, Naples, Italy
[b] Department of Biomedical and Neuromotor Sciences, DIBINEM, University of Bologna, Alma Mater Studiorum, Via San Vitale 59, 40125, Bologna, Italy
[c] Department of Neurosciences, Reproductive and Odontostomatological Sciences, Oral Medicine Unit, School of Medicine, University "Federico II" of Naples, Via Pansini 5, 80131, Naples, Italy

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ABSTRACT

Objectives: This paper aimed to provide a literature review of the mechanical and biological properties of zirconia-reinforced lithium silicate glass-ceramics (ZLS) in Computer-aided design / Computer-aided manufacturing (CAD/CAM) systems.
Data/Sources: An extensive search of the literature for papers related to ZLS was made on the databases of PubMed/Medline, Scopus, Embase, Google Scholar, Dynamed, and Open Grey. The papers were selected by 3 independent calibrated reviewers.
Study selection: The search strategy produced 937 records. After the removal of duplicates and the exclusion of papers that did not meet the inclusion criteria, 71 papers were included.
Conclusions: After reviewing the included records, it was found that two types of ZLS (Vita Suprinity PC; Vita Zahnfabrik and Celtra Duo; Dentsply Sirona) are nowadays available on the market for CAD/CAM systems, similar in their chemical composition, microstructure, and biological-mechanical properties. ZLS is reported to be a biocompatible material, whose fracture resistance can withstand physiological chewing loads. The firing process influences the improvements of strength and fatigue failure load, with a volumetric shrinkage.
To date, ZLS can be considered a viable alternative to other glass-ceramics for fixed single restorations.
Clinical Significance: . As to biocompatibility and mechanical properties of ZLS, data are still scarce, often controversial and limited to short-term observational periods. These promising ceramics require further *in vitro/ in vivo* studies to accurately define mechanical and biological properties, mainly in the long-term performance of restorations produced with such materials.

1. Introduction

The research and development of new restorative materials aimed at getting high mechanical and esthetic performances has led to the introduction on the market of zirconia-reinforced lithium silicate ceramics (ZLS), that can be employed with Computer-aided design / Computer-aided manufacturing (CAD/CAM) technologies.

ZLS was developed by two companies, Vita (Vita Zahnfabrik, H. Rauter GmbH & Co., Bad Säckingen, Germany) and Dentsply (Dentsply Sirona, DeguDent, GmbH, Hanau-Wolfgang, Germany), in conjunction with the Fraunhofer Institute for Silicate Research (Würzburg, Germany), separately marketed as different products: Vita Suprinity PC and Celtra Duo [1–3]. These materials exhibit similar microstructures: a homogeneous glassy matrix contains a crystalline component made of

Abbreviations: CAD/CAM, Computer-aided design/Computer-aided manufacturing; FC, feldspathic ceramics; FEA, finite element analysis; HGFs, human gingival fibroblasts; LS_2, lithium disilicate ceramics; PICN, polymer-infiltrated ceramic networks; PMMA, polymethyl methacrylate; RNC, resin nanoceramic; SEM, Scanning Electron Microscope; HT-Z, high translucent zirconia ceramics; ZLS, zirconia-reinforced lithium silicate ceramics.

* Corresponding author at: Department of Neurosciences, Reproductive and Odontostomatological Sciences, Division of Prosthodontics and Digital Dentistry, University "Federico II" of Naples, Via Pansini 5, 80131, Naples, Italy.

E-mail addresses: zarone@unina.it (F. Zarone), gennaro.ruggiero2@unina.it (G. Ruggiero), renato.leone@unina.it (R. Leone), lorenzo.breschi@unibo.it (L. Breschi), stefania.leuci@unina.it (S. Leuci), roberto.sorrentino@unina.it (R. Sorrentino).

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round and submicrometric elongated grains of lithium metasilicates and lithium orthophosphates; in addition to these, tetragonal zirconia fillers are added, aimed at increasing strength values. After a crystallization process, lithium disilicate grains are generated. Lithium metasilicate is reported to be grown larger in Celtra Duo than in Suprinity (up to ~1 and ~0.5 μm in length, respectively) [2–6].

This structural typology has been developed in order to combine favorable optical properties with increased mechanical characteristics, compared to other glass-ceramics, although, to date, this assumption is still controversial [4,7–13].

ZLS blanks are available in a pre-crystallized or crystallized form. The crystallization process, inside a dental furnace, allows the nucleation of the crystals, with a subsequent improvement of their mechanical properties compared to the pre-crystallized ones [2]. Furthermore, the fracture resistance was reported to withstand physiological occlusal forces, and it increases after one firing protocol [14].

Due to its high translucency and biaxial flexural strength values, ZLS was tested for tooth- and implant-supported single partial and full restorations in both anterior and posterior regions [4,15,16], as well as for occlusal veneers [7,17]. It was also tested for endocrowns [18,19], although the reported results are not satisfactory.

Some findings showed that the machinability of ZLS is worse than the one of LS_2 [4,20], so that ZLS was defined "the most difficult to machine among glass ceramics" [20].

Also, ZLS is acid sensitive [21], and it is important to clarify what the ideal acid concentration and etching times are; moreover, the best cements polymerization (dual- or light-curing) and whether it is worth silanizing ZLS.

ZLS is also reported to be a biocompatible material [2], but to date, there is no univocal evidence about *in vitro* data regarding cell proliferation.

To date, the biological and mechanical performances of ZLS need a more in-depth look from a scientific point of view, in order to formulate a clear definition of their clinical indications and limitations. With the purpose of shedding light on the mechanical and biological properties of ZLS in CAD/CAM systems, this literature review is focused on the chemical composition, microstructure, biocompatibility, physico-mechanical properties, and marginal/internal fit of ZLS-based restorations.

2. Methods

2.1. Search strategy

An extensive search of the literature for papers related to ZLS was performed on the databases of PubMed/Medline, Scopus, Embase, Google Scholar, Dynamed, and Open Grey.

The literature search was performed using combinations of the keywords "zirconia-reinforced lithium silicate" or "ZLS". The following queries were used for each electronic database:

- PubMed/Medline, Google Scholar, and Open Grey = "(zirconia-reinforced lithium silicate) or (zls)" was added into each query box.
- Dynamed = ZLS; zirconia-reinforced; zirconia-reinforced lithium silicate; zirconia lithium.
- Scopus = (TITLE-ABS-KEY (zirconia-reinforced AND lithium AND silicate) OR TITLE-ABS-KEY (zls)).
- Embase = 'zirconia-reinforced lithium silicate' OR ('zirconia reinforced' AND ('lithium'/exp OR lithium) AND ('silicate'/exp OR silicate)) OR zls.

The references of the found records were imported as a Research Information Systems file into Mendeley (Mendeley Ltd., London, UK) in order to remove the duplicates.

2.2. Inclusion and exclusion criteria

Studies were considered as appropriate for the present literature review if they met the following inclusion criteria: 1) studies focused on the biocompatibility and/or mechanical properties of ZLS for CAD/CAM systems; 2) studies performed *in vitro*, *in silico,* or *in vivo*; 3) case reports; 4) systematic reviews.

The following exclusion criteria were used: 1) studies performed on non-human animals; 2) studies not addressed to the dentistry field; 3) studies referred to ZLS restorations produced by heat-pressed ceramics process.

No limitations were applied to the publication date or the language of the papers.

2.3. Data extraction

With the purpose of shedding light on the mechanical and biological characteristics of ZLS, the following variables were extracted:

1. Chemical composition and microstructure;
2. Biocompatibility;
3. Physico-mechanical values of ZLS;
4. Laboratory and post-milling manual processing;
5. Minimal thickness;
6. Fracture patterns and plastic deformation;
7. Fatigue failure load;
8. Marginal and internal fit.

According to the inclusion criteria, 3 calibrated researchers (F.Z., R. S, and G.R.) independently selected the articles reading the titles, abstracts, and keywords. The full text of each identified article was read to determine whether it was suitable for inclusion. In case of disagreement among the investigators, a majority criterion would have been used (*i.e.*, 2 out of 3).

The workflow of the paper screening process is reported in Fig. 1, according to the "PRISMA 2009 Flow Diagram" [22].

2.4. Calibration process

As regards the recorded titles and abstracts, the 3 reviewers performed pilot calibration exercises on a common random group of 20 references, applying the inclusion and exclusion criteria. After the exercise, the reviewers discussed which references were included or excluded. The reviewers aimed to reach an agreement on at least 90 % of the papers. The process would have been repeated until they had obtained the predetermined agreement level before starting the screening of the whole set of titles and abstracts collected. Also, the calibration process, with the same agreement level, was used on a random sample of 8 papers for the full-text screening of the included articles after reading titles and abstracts.

3. Results

3.1. Data synthesis

The literature search was completed in February 2021 and the included studies were published between 2015 and January 2021.

The search strategy produced 937 records, many of which were duplicates: 188 from PubMed/Medline, 239 from Scopus, 175 from Embase, 294 from Google Scholar, 41 from Dynamed, and 0 from Open Grey. All the duplicates were removed, thus all the selected databases produced 281 records. After the examination of titles, abstracts, and keywords, the reviewers excluded 180 records, because they did not meet the inclusion criteria. As to the remaining 101 records, 30 more were excluded after a full-text analysis because they did not provide considerable information about ZLS for dental research and clinical

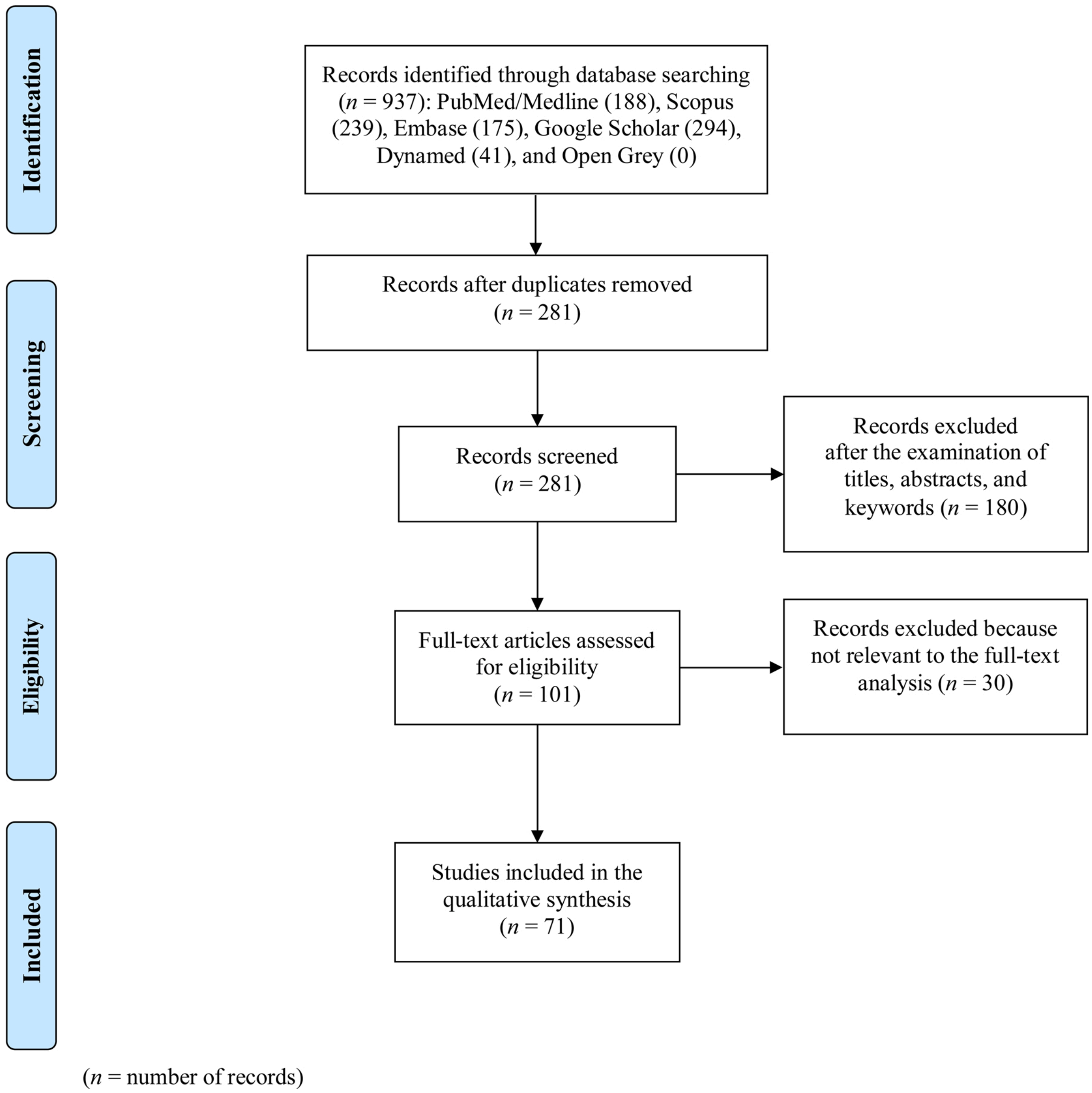

Fig. 1. Title: Search flowchart as described in the PRISMA guidelines.
Caption: (n = number of records).

practice. The remaining 71 records were included in the present literature review (Table 1).

No systematic reviews or case reports were found.

The reviewers obtained an agreement level superior to 90 % after the first calibration exercise on titles and abstracts screening and an agreement level of 100 % on full-text papers screening after only one exercise.

No disagreement was pointed out among the search investigators about the included records.

3.2. Chemical composition and microstructure

ZLS-based materials, to date marketed as Celtra Duo (Dentsply Sirona, DeguDent, GmbH, Hanau-Wolfgang, Germany) and Suprinity (Vita Zahnfabrik, H. Rauter GmbH & Co., Bad Säckingen, Germany), showed very similar microstructures, mainly consisting of two ~70 vol. % crystallized phases: one is made of larger, submicrometric lithium metasilicate crystallites (Li_2SiO_3) in slightly elongated shapes, more rounded than lithium disilicate ceramics (LS_2) needle-shaped ones; the other is made of smaller nanometric lithium orthophosphate crystallites (Li_3PO_4) as round granules [6]. After crystallization firing, a significant increase was observed for both phases and a new crystal phase appears, namely lithium disilicate ($Li_2Si_2O_5$), crystallized from the glassy matrix; such a crystallization is allowed by the presence of diphosphorus pentoxide (P_2O_5) as nucleation agent [6].

Lithium metasilicate crystallites in the glassy phase show different dimensions in Celtra Duo (about 1 μm) compared to Suprinity (about 0.5 μm) [6,12,23], in both cases smaller than LS_2 crystals, the latter described as elongated, needle-shaped, with length comprised between 0.5 and 4 μm [24,74]. It has been suggested that such a difference in size between the two different brand formulations could be due to discrepancies in the processing parameters, like firing temperature and time, being Suprinity treated with an additional and shorter crystallization firing process compared to Celtra Duo [5,6].

X-ray diffraction analysis on Suprinity showed crystallization peaks corresponding to lithium monosilicate, aluminum silicate, and tetragonal zirconia [24].

Raman analysis in pre-crystallized ZLS confirmed the presence of crystal phases made of lithium metasilicate and lithium orthophosphate; post-crystallization, besides an increase in intensity related to these

Table 1
An overview of the 71 included records and the variables for inclusion regarding each paper.

Analyzed variables	Authors (Year of publication)
Chemical composition or microstructure	Riquieri et al. (2018) [1], Vita Zahnfabrik (2019) [2], Dentsply Sirona Inc. (2016) [3], Elsaka and Elnaghy (2016) [4], Belli et al. (2018) [5], Belli et al. (2017) [6], Vasiliu et al. (2020) [12], Sen and Us (2018) [15], Wendler et al. (2017) [23], Ramos et al. (2016) [24], De Mendonca et al. (2019) [25], Traini et al. (2016) [26]
Biocompatibility	Vita Zahnfabrik (2019) [2], Rizo-Gorrita et al. (2018) [27], Rizo-Gorrita et al. (2019) [28], Dal Piva et al. (2018) [29], De Luca et al. (2018) [30], Abdalla et al. (2018) [31]
Physico-mechanical values of ZLS	Elsaka and Elnaghy (2016) [4], Belli et al. (2018) [5], Belli et al. (2017) [6], Al-Akhali et al. (2017) [7], Hamza and Sherif (2019) [8], Gomes et al. (2017) [9], Kashkari et al. (2019) [10], Schwindling et al. (2017) [11], Zarone et al. (2020) [13], Sen and Us (2018) [15], Preis et al. (2017) [16], Von Maltzahn et al. (2018) [17], Taha et al. (2018) [18], El Ghoul et al. (2019) [19], Chen et al. (2020) [20], Wendler et al. (2017) [23], Ramos et al. (2016) [24], De Mendonca et al. (2019) [25], Nishioka et al. (2018) [32], Guilardi et al. (2020) [33], Choi et al. (2017) [34], Zimmermann et al. (2017) [35], Preis et al. (2015) [36], Jassim and Majeed (2018) [37], Rosentritt et al. (2017) [38], Yeğin and Atala (2020) [39], Yilmaz et al. (2020) [40], Kermanshah et al. (2020) [41], Dartora et al. (2020) [42], Liu et al. (2021) [43], Juntanvee and Uasuwan (2020) [44], Srichumpong et al. (2019) [45], Monteiro et al. (2018) [46], Ottoni et al. (2018) [47], Lawson et al. (2016) [48]
Laboratory or post-milling manual processing	Riquieri et al. (2018) [1], Passos et al. (2019) [14], Traini et al. (2016) [26], Lawson et al. (2016) [48], Schweitzer et al. (2020) [49], Alao and Bujang (2021) [50], Badawy et al. (2016) [51], Aurèlio et al. (2017) [52], Romanyk et al. (2020) [53], Passos et al. (2018) [54], Kang et al. (2020) [55], Alves et al. (2019) [56]
Minimal thickness	Choi et al. (2017) [34], Zimmermann et al. (2017) [35], Monteiro et al. (2018) [46], Sieper et al. (2017) [57], Bergamo et al. (2019) [58], Shaik and Alfarsi (2019) [59], Tribst et al. (2018) [60], Alammari et al. (2018) [61]
Fracture patterns and plastic deformation	Ramos et al. (2016) [24], De Mendonca et al. (2019) [25], Liu et al. (2021) [43], Monteiro et al. (2018) [46], Sieper et al. (2017) [57], Bergamo et al. (2019) [58], Abu-Izze et al. (2018) [62], Diniz et al. (2020) [63]
Fatigue failure load	Von Maltzahn et al. (2018) [17], Monteiro et al. (2018) [46], Ottoni et al. (2018) [47], Alammari et al. (2018) [61], Diniz et al. (2020) [63], Al-Akhali et al. (2019) [64], Venturini et al. (2019) [65], Alves et al. (2020) [66], Schlenz et al. (2020) [67], Dal Piva et al. (2020) [68]
Marginal and internal fit	Vita Zahnfabrik (2019) [2], Gomes et al. (2017) [9], Taha et al. (2018) [18], El Ghoul et al. (2019) [19], Preis et al. (2015) [36], Alammari et al. (2018) [61], Hasanzade et al. (2020) [69], Dentsply Sirona Inc. (2017) [70], Zimmermann et al (2019) [71], Falahchai et al. (2020) [72,73]

components, the new crystal phase of lithium disilicate was also observed [6].

In a microstructural comparison, LS_2 is characterized by interlocking needle-shaped crystals embedded in a glassy matrix, while ZLS shows a homogeneous fine crystalline structure with rounded and rod-like crystals. The percentage of the crystalline phase is higher in LS_2 [4,24,25]. Actually, as found in CAD/CAM LS_2, in ZLS the presence of both lithium metasilicate and disilicate grains has been evidenced in the final stage of crystallization [5,6,75–77].

The chemical composition of ZLS-based materials is specified in Table 2, as reported by various sources in the literature.

3.3. Biocompatibility

In the present state of knowledge, data regarding the biocompatibility of ZLS are scarce and controversial. Suprinity was deemed biocompatible by the "North American Science Associates Inc." (NAMSA) from specific evaluations based on cytotoxicity, sensitization, subchronic systemic toxicity, irritation, and genotoxicity [2].

Human gingival fibroblasts (HGFs) cultured onto ZLS exhibited lower cell proliferation, coverage, and spreading than onto zirconia; such a worse cellular response in ZLS could be attributed to a rougher and less homogeneous surface topography [27]. In a comparative *in vitro* study, ZLS and zirconia showed intermediate values of cell viability and collagen secretion between LS_2, which exhibited the best values, and polymethyl methacrylate (PMMA), which showed the lowest values [28].

Furthermore, polished ZLS surfaces have been reported to be less rough, accumulating less biofilm and displaying higher surface free energy than glazed surfaces; however, polished surfaces showed severe initial cytotoxicity for HGFs but were inert in the long term; such cytotoxicity (24 h) may be related to an initial release of remnants of the

Table 2
Analysis of ZLS chemical composition (in weight %).

Vita Suprinity® PC. Technical and scientific documentation. 2019 [2]	Silicon dioxide (56−64); Lithium oxide (15−21); Zirconia (8−12); Phosphorus oxide (3−8); Potassium oxide (1−4); Aluminium oxide (1−4); Pigments (0−6); Cerium dioxide (0−4).
Celtra® Duo. Zirconia-Reinforced Lithium Silicate (ZLS) Block. Technical Monograph. 2016 [3]	Silicon dioxide (58.0); Lithium oxide (18.5); Zirconia (10.1); Phosphorus oxide (5.0); Cerium dioxide (2.0); Aluminium oxide (1.9); Terbium Oxide (1.0).
Traini et al. 2016 [26], about Suprinity fired	Silicon (59); Lithium (20); Zirconium (12); Phosphorus (4.2); Potassium (2.5); Aluminium (1.5); Other minor components (0.8).
Ramos et al. 2016 [24], about Suprinity fired	Oxygen (51.2); Silicon (29.6); Zirconia (15.5); Potassium (2.3); Aluminium (1.3).
Riquieri et al. 2018 [1], about Suprinity fired	Oxygen (52.60); Silicious (30.95); Zirconium (13.00); Potassium (2.06); Aluminium (1.35).
Riquieri et al. 2018 [1], about Celtra Duo fired	Oxygen (53.09); Silicious (30.85); Zirconium (12.50); Potassium (2.36); Aluminium (1.17).
Sen and Us. 2018 [15], about Suprinity fired	Oxygen (52.1); Silicon (27.52); Zirconium (15.7); Potassium (2.34); Aluminium (1.28); Carbon (1.05).

polishing material, reducing its cytotoxic effect after 7 days. Over time, the cells strengthen their defense mechanisms and become able to protect themselves [29].

Another *in vitro* study showed that proliferation and viability of HGFs onto crystallized, not polished and polished ZLS, before and after crystallization, are similar to those of zirconia ceramics, with favorable biological properties suggesting an indication for use in implant-supported restorations with margins in contact with peri-implant tissues [30].

In the case of polished surfaces, ZLS demonstrated the lowest bacterial adhesion, compared to LS_2 and feldspathic ceramics (FC) [31].

3.4. Physico-mechanical properties

3.4.1. Physico-mechanical values of ZLS

According to several reports, it can be stated that in ceramic materials the lower the glassy content, the higher the dental ceramic overall strength [23,24,32,33]. In the last decade, ZLS was introduced on the market with the purpose of offering at the same time advanced esthetic properties, being a translucent glass-ceramic with silicate crystals embedded in a high content of glassy matrix, together with a favorable mechanical behavior, thanks to the addition of tetragonal zirconia fillers, exploiting a mechanism of crack interruption [4].

In the last years, several studies have proved that ZLS restorations show fracture resistance values exceeding the physiological occlusal/masticatory forces [7,9,34–36], although the concept of zirconia fillers acting as an additional toughening mechanism [20,78], at the basis of the material physico-chemical formulation, has been confuted by some authors [24]. It has always to be considered that, due to the wide heterogeneity of research designs and testing modalities, *in vitro* data are not infrequently controversial, making their comparisons very difficult and possible correlations to *in vivo* biomechanical behavior not always easy.

According to some research data, in a comparison with other restorative materials, occlusal veneers made of LS_2 and ZLS showed higher resistance to fracture than those fabricated with polymer-infiltrated ceramic networks (PICN) and PMMA [7]. In another study, the load at fracture of ZLS tabletops was found to be significantly higher than that of feldspar-based ceramic ones [17]. Besides, similar results were reported by a research conducted on monolithic, crown-shaped restorations, showing higher fracture strength of LS_2 and ZLS compared to PICN and a hybrid high-performance polymer composite resin [25].

Compared to bilayered, ceramic-veneered zirconia restorations, monolithic crowns made of LS_2 and ZLS were reported to exhibit higher fracture resistance [8].

To date, several studies have been carried out in order to compare the mechanical properties of the two most popular silicate-based materials, LS_2 and ZLS, although the reported data are not always in agreement.

According to some *in vitro* investigations [4,8,11,15,37], ZLS exhibited higher mechanical performances than LS_2, confirming the possible efficiency of the zirconia additional phase in increasing resistance thanks to a mechanism of crack interruption. In some studies, compared to LS_2, the material showed higher fracture [8,37] and flexural strength [4,15]. In another research, carried out on monolithic crowns in the anterior sites, load-to-failure values were reported to be slightly higher for glazed ZLS than for LS_2; after submitting the restorations to an extensive thermocycling test, such a fracture resistance was still maintained by ZLS specimens [11].

ZLS has also been tested *in vitro* as a material for implant-supported molar crowns, reporting high fracture forces, although lower than those shown by zirconia [16]. In any case, the insertion of a screw channel might reduce the stability of ZLS restorations [38].

On this topic, other studies report fewer positive results. In an *in vitro* investigation, high strength zirconia crowns showed the most favorable load-to-fracture values, followed by LS_2 and ZLS, the latter exhibiting significantly lower mechanical performance [10]. Also, fatigue strength, evaluated by biaxial flexural test on disc-shaped specimens, exhibited the highest values with high translucence yttrium stabilized tetragonal zirconia, followed, in decreasing order by LS_2, ZLS, PICN, and FC [32].

Other investigations reported lower values for fracture [9] and failure [39] loads in implant-supported ZLS monolithic crowns compared to LS_2 ones.

Moreover, in a recent study, no differences were detected among ZLS, PICN, LS_2, and zirconia as to strains around the implant platform, none of these materials offering a significant load absorption aimed at minimizing the strains generated at the platform level. [40].

In ceramic inlay-retained fixed partial dentures, the fracture load of zirconia was reported to be higher than that of ZLS [41].

In the last decade, the concept of endocrown has been gaining more and more popularity for the restoration of endodontically treated teeth, utilizing mechanical retention offered by the pulp chamber together with chemical/micromechanical adhesion provided by bonding procedures. In posterior endocrowns, LS_2 resistance to fracture was reported to be higher compared to ZLS, both under axial [19] and lateral forces [18,19]. According to a recent *in vitro* and finite element analysis (FEA) study, the highest fracture strength resistance values were exhibited by monolithic endocrowns made of zirconia, compared to LS_2, ZLS, and leucite reinforced ceramics, although monolithic zirconia and ZLS showed worse failure modalities, with a higher rate of catastrophic fractures [42].

The physico-mechanical values collected from different studies are shown in Table 3.

It is more than evident that, in order to get a deeper insight about the mechanical properties of this material, data reported by *in vitro* studies should be furtherly corroborated by *in vivo* results of clinical, long-term, controlled and randomized trials, that are missing, at the moment, in the scientific literature.

3.4.2. Laboratory and post-milling manual processing

Several studies have been carried out on the modifications of the physico-mechanical properties of ZLS following laboratory manufacturing, particularly sintering and crystallization. In this regard, an evident increase of the following ZLS physical values was shown after the firing process: modulus of elasticity, flexural strength, fracture toughness, hardness, and characteristic strength [1,26,48–51], simultaneously with a decrease of the Weibull modulus and a significant shrinkage [1,49], as reported in Table 4. The material seemed to be brittler with a tendency to develop inner cracks at the partially crystallized state; for this reason, particular care should be taken during the manipulation process for marginal adaptation [26].

The increase of ZLS restoration strength after one firing protocol was confirmed by Passos et al. [14]. Moreover, an extended glaze firing protocol has been proposed, based on the same initial pre-heating time, temperature, and temperature increase rate as the conventional manufacturer-recommended glaze firing, with a difference, in that the extended glaze firing differs by slow cooling until the temperature drops to 200 °C in a closed furnace for a dwell time of 15 min [52]. This extended glaze firing protocol, after hard machining of ZLS, repaired defects by generating beneficial compressive residual stress, differently from conventional glaze firings, that can create tensile stresses [52].

The surface defects related to machining procedures negatively influence the mechanical performance of ZLS fabricated with CAD/CAM technologies; in this regard, the post-machining heat treatment can partially relieve the strength-limiting damage caused by CAD/CAM procedures [53].

After the final processing of the ZLS restorations, a manual adjustment of occlusal morphology should be avoided, because it has been demonstrated that this procedure can decrease the fracture load of ZLS crowns [54].

As for the milling accuracy, ZLS showed lower mean values than LS_2;

Table 3
Physico-mechanical values of ZLS (mean ± SD).

Authors (Product name)	Modulus of Elasticity (GPa)	Flexural Strength (MPa)	Fracture toughness = K_{Ic} (MPa $m^{1/2}$)	Vickers' Hardness (GPa)	Characteristic Strength (MPa)	Weibull modulus (m)	Poisson's ratio	Fracture Resistance (N)	Density (g/cm^3)
Liu et al. 2020 [43] (Celtra Duo)					279	2.7			
Juntavee and Uasuwan 2020 [44] (Suprinity)		218.43 ± 38.46			234.23	6.40			
De Mendonca et al. 2019 [25] (Suprinity)		230 ± 20		6.78 ± 0.013 *					
Srichumpong et al. 2019 [45] (Suprinity and Celtra Duo)			1.86 (Suprinity) 1.75 (Celtra Duo)	6.8 (Same value both for Suprinity and Celtra Duo)					
Monteiro et al. 2018 [46] (Celtra Duo)							0.30		
Von Maltzahn et al. 2018 [17] (Celtra Duo)								1,571.1 ± 297.0	
Ottoni et al. 2018 [47] (Suprinity)		179 ± 56	1.93 ± 0.32	6.67 ± 0.18	197 (158; 200)	4 (3;5)			
Nishioka et al. 2018 [32] (Suprinity)					152.1 ± 7.5				
Jassim et al. 2018 [37] (Celtra Duo)								1404.5 ± 236.51	
Sen and Us. 2018 [15] (Suprinity)		510 ± 43			532	8.8			
Belli et al. 2018 [5] (Suprinity and Celtra Duo)			1.40 ± 0.10 (Suprinity) 1.52 ± 0.05 (Celtra Duo)						
Schwindling et al. 2017 [11] (Celtra Duo)								725 ± 162	
Belli et al. 2017 [6] (Suprinity and Celtra Duo)	105.8 (Suprinity) 108.2 (Celtra Duo)						0.207 (Suprinity) 0.224 (Celtra Duo)		2.643 (Suprinity) 2.630 (Celtra Duo)
Wendler et al. 2017 [23] (Suprinity and Celtra Duo)	104.9 (Suprinity) 107.9 (Celtra Duo)				611.24 (573.80;651.58) (Suprinity) 626.84 (587.74;669.02) (Celtra Duo)	5.29 (3.96;6.45) (Suprinity) 5.19 (3.89;6.33) (Celtra Duo)	0.208 (Suprinity) 0.222 (Celtra Duo)		
Hamza et al. 2017 [8] (Suprinity)								1742.9 ± 102.7	
Ramos et al. 2016 [24] (Suprinity)	65.6 ± 4.1		1.25 ± 0.79		217.5 (151.84;238.6)	10.0 (C.I. 6.92–14.41)	0.23 ± 0.03		1.60
Lawson et al. 2016 [48] (Celtra Duo)	61.0 ± 10.0	300.1 ± 16.8		4.54 ± 0.26*					
Elsaka and Elnaghy 2016 [4] (Celtra Duo)	70.44 ± 1.97	443.63 ± 38.90	2.31 ± 0.17	6.53 ± 0.46	460.74	13.41			

* The numerical values of Vickers' Hardness were different from the ones reported in the corresponding original papers. This change had the goal to report numerical values converted to the same unit (GPa).

Table 4
Physical values (mean ± SD) of unfired/fired ZLS.

	Modulus of Elasticity (GPa)	Flexural Strength (MPa)	Fracture toughness = K_{Ic} (MPa $m^{1/2}$)	Vickers' Hardness (GPa)*	Weibull Modulus (m)	Characteristic Strength (MPa)
Schweitzer et al. 2020 [49] (Celtra Duo)		189.02 ± 25.5 / 252.86 ± 53.78			8.9 / 5.81	219.3 / 314.35
Alves et al. 2019 [56] (Suprinity and Celtra Duo)	89.8 ± 5 / 97 ± 6.2 (Suprinity) 92 ± 4.7 / 98.9 ± 3.8 (Celtra Duo)		1.15 ± 0.13 / 1.39 ± 0.04 (Suprinity) 1.4 ± 0.12 / 1.49 ± 0.05 (Celtra Duo)	6.34 ± 0.33/ 6.5 ± 0.11* (Suprinity) 6.64 ± 0.17 / 6.63 ± 0.14* (Celtra Duo)		
Riquieri et al. 2018 [1] (Suprinity and Celtra Duo)			2..21 ± 0.11 / 2.63 ± 0.14 (Suprinity) 2.26 ± 0.80 / 2.51 ± 0.59 (Celtra Duo)	597.533 ± 33.97 / 683.267 ± 16.07 (Suprinity) 682.400 ± 15.31 / 693.333 ± 10.85 (Celtra Duo)	7.07 / 5.38 (Suprinity) 5.86 / 5.77 (Celtra Duo)	106.95 / 191.02 (Suprinity) 163.86 / 251.25 (Celtra Duo)
Lawson et al. 2016 [48] (Celtra Duo)	61.0 ± 10.0 / 63.6 ± 3.3	300.1 ± 16.8 / 451.4 ± 58.9		4.546 ± 0.26* / 5.836 ± 0.36*		
Traini et al. 2016 [26] (Suprinity)			2.8 ± 0.9 / 4.7 ± 0.8	6.8 ± 0.5 / 7.6 ± 0.7		

* The numerical values of Vickers' Hardness were different from the ones reported in the corresponding original papers. This change had the goal to report numerical values converted to the same unit (GPa).

nevertheless, the milling accuracy of ZLS was within 120 μm, therefore considered clinically acceptable [55].

3.4.3. Minimal thickness

Thickness is a paramount factor in all-ceramic restorations, both from a clinical and technical point of view, in that it affects the design of the tooth preparation and, at the same time, strongly influences fracture resistance and survival rate of the prosthesis.

In ZLS, as expected, mean fracture loads of monolithic restorations were reported to increase significantly as thickness increased [34,35,57].

According to an *in vitro* study, at a thickness of 1.5 mm Suprinity exhibited a fracture resistance similar to LS_2 and higher than PICN and Celtra Duo [34]; conversely, another paper reported higher mean fracture loads for LS_2 than for ZLS at both 1.5 mm and 1.0 mm thickness [35]. Another research showed promising durability of ZLS single crowns for the thickness of 1.0 mm [57]; at such a thickness, fracture resistance values of ZLS, LS_2, and PICN were shown to be similar [34]. At 0.5 mm thickness, a substantially reduced mechanical resistance was evidenced for most metal-free, silicate-based, feldspathic, and hybrid materials [35,58]; on the contrary, another research, aimed at comparing fracture resistance of full-coverage minimally invasive crowns made of ZLS, PICN, and high translucent zirconia ceramics (HT-Z), showed that with minimal thickness of 0.6 mm restorations made of HT-Z and PICN were mechanically resistant within the range of biting forces, while ZLS exhibited the lowest load values [59].

FEA studies have been increasingly carried out in the last decade on the topic of metal-free materials, allowing an "*in silico*" reliable evaluation of mechanical behavior of dental restorations. In a research on stress distribution in occlusal veneers, a direct correlation between restoration thickness and concentration of tensile stresses was detected, in the following decreasing order for the simulated materials: HT-Z (highest stress concentration), LS_2, FC, ZLS, and PICN [60]. Moreover, the typology of restorative material differently influenced the concentration of stress on the cement layer, in the following decreasing order: PICN > HT-Z > ZLS > LS_2 > FC. In the same study, the cement layer thickness was not shown to be relevant to mechanical resistance.

In another FEA investigation, higher stress concentrations on the cement interface were detected reducing ceramic thickness [46].

As regards the influence of preparation design on ZLS mechanical resistance, it has been evidenced that an increase in total occlusal convergence from 12° to 20° resulted in higher load-to-fracture values of ZLS crowns and did not influence their internal and marginal fit [61].

3.4.4. Fracture patterns and plastic deformation

Some fractographic studies have been carried out in order to shed light on mechanical behavior and failure patterns of ZLS restorations.

Silicate-based materials like ZLS and LS_2 are showed to suffer mainly from unrepairable and catastrophic fracture patterns, differently from hybrid ceramics, in which limited chipping and type II fracture patterns (*i.e.*, affecting less than half the crown) are more commonly found [25].

Light microscopy showed that ZLS failures consisted primarily of bulk fractures starting from the cementation surface as radial cracks propagating to the cervical area [46,58,62,63]. It has also been evidenced that both ZLS and LS_2 are susceptible to slow crack propagation, which is one of the main causes of failure in metal-free prostheses [24].

ZLS and LS_2 have been reported to show similar susceptibility to subcritical crack growth, a phenomenon more limited for zirconia thanks to its phase transformation known as transformation toughening [43]; in another study, an effective mechanism of crack interruption was confirmed in ZLS by the presence of clear semicircular arrest lines at scanning electron microscope (SEM), close to the origin of failure [57].

3.4.5. Fatigue failure load

To date, it has been demonstrated that load-at-fracture resistance of ZLS makes this material suitable for clinical purposes; cyclic loading simulating 1 year of use (*i.e.*, 10^6 cycles at 4 Hz and a load of 88 N) did not result in ZLS crowns fatigue failure [61]. As regards the effects of thermal aging, the results reported in the literature are still controversial; in an investigation, experimental aging (*i.e.*, 10^6 cycles at 2.5 Hz and a load of 50 N with thermal aging of 10,000 cycles at 5−55 °C) did not compromise the mechanical stability of the material [17], conversely, in another study, aging (induced according to staircase method with 100,000 cycles at 20 Hz and thermal aging of 10,000 cycles in 5−55 °C) determined a reduction in fatigue failure load [63]. Furthermore, it was reported that thermo-mechanical fatigue reduced the survival rate and fracture strength of ZLS occlusal veneers bonded to enamel using the self-etching technique [64].

Several investigations evaluated the fatigue failure load of ZLS, with different experimental designs [46,47,65]. An *in vitro* study using the boundary and staircase fatigue methods showed that, after 10^3 cycles, a degradation of 78 % of the initial strength occurred for both fatigue methods; differently, when the number of cycles increased from 10^3 to 10^4, there was no further significant degradation [47].

In another research, fatigue failure loads for ZLS, determined using the staircase method (*i.e.*, 100,000 cycles at 20 Hz) at ceramic thicknesses ranging from 1.0–2.5 mm, showed the following values: Suprinity = 716.5 ± 95.5 N (at 1.0 mm) up to 1119.6 ± 241.7 N (at 2.5 mm); Celtra Duo = 404.0 ± 43.3 N (at 1.0 mm) up to 1126.8 ± 80.2 N (at 2.5 mm). From these results, it can be asserted that different ZLS thicknesses affect the fatigue failure load of the bonded system so that the thicker the ZLS, the higher the expected fatigue failure load. Moreover, the staircase experimental procedure confirmed that the firing procedures (glaze firing process or crystallization firing) improved the fatigue failure load [63].

Comparisons among the fatigue behavior of ZLS and other materials have shown conflicting results among different studies, perhaps due to the different fatigue test designs performed.

Comparative *in vitro* studies between ZLS and other materials showed that CAD/CAM posterior ZLS crowns exhibited better fatigue resistance than LS_2 but worse than monolithic crowns made of translucent zirconia [66]. In a different analysis performed with the optical coherence tomography, ZLS showed the highest horizontal and vertical fatigue damages, followed by PICN, resin composites, and 5 mol% Y_2O_3-partially stabilized zirconia [67].

Another *in vitro* investigation reported that the fatigue behavior of ZLS was similar to LS_2 and leucite ceramics, better than FC and PICN but worse than resin nanoceramic (RNC); in the same study, the fatigue failure load evaluated by a step-stress approach (*i.e.*, 400 N–2200 N; step-size of 200 N; 10,000 cycles per step; 1.4 Hz) reached 1013.33 N after 40,666 cycles for ZLS [65].

These results do not clarify whether the fatigue behavior of ZLS is better than LS_2, but it should be noted that RNC [65] and resin composites [67] expressed better fatigue performance than ZLS, due to the superior flexibility and reduced brittleness, probably determined by the resinous content in their microstructure [65]. In any case, compared to zirconia, it is clear that ZLS is less efficient even in fatigue behavior [66, 67].

Surface morphology is a factor that seems to affect fatigue behavior; in fact, ZLS presented higher survival probability and fatigue strength when polished than when showing a roughened surface [68]; in support of these results, another *in vitro* study reported that higher degrees of roughness (*i.e.*, Ra = 1.98 μm; Rz = 12.25 μm) had a negative influence on the fatigue performance of ZLS [33].

3.5. Marginal and internal fit

ZLS crowns were proved to offer clinically acceptable internal and marginal gaps (≤150 μm) [9,18,19,36,69]. This is in agreement with manufacturers' documentations reporting good edge stability at a thickness of 160−200 μm [2,70]. Nevertheless, higher levels of marginal misfit were reported for ZLS implant-supported crowns compared to LS_2 CAD/CAM ones in an *in vitro* study [9].

As regards design preparation, it has been demonstrated that marginal and internal adaptation of ZLS crowns is not significantly affected by the parameter of total occlusal convergence, in a range comprised from 12° to 20° [61]. With regard to ZLS overlay restorations, a preparation design characterized by anatomical occlusal reduction with rounded shoulder and a central groove exhibited poorer marginal adaptation than one with anatomical occlusal reduction alone [71]. This latter preparation design also showed the highest fracture resistance (2737.95 ± 409.66) [72].

As regards endocrown restorations, the following, not exciting, mean values of fit were reported for ZLS: margin = 131.0 μm, axial = 160.8 μm, and occlusal = 182.3 μm [73]; internal and marginal adaptation of endocrowns were not demonstrated to be significantly different among ZLS, LS_2, and PICN [69].

4. Conclusions

According to the present literature review, in the current state of knowledge, the following conclusions can be drawn for the mechanical and biological properties of ZLS CAD-CAM:

- Despite the presence of zirconia grains in the glassy matrix, there is no undisputed evidence confirming a higher mechanical strength compared to LS_2. The fracture resistance was reported to withstand physiological occlusal forces. At 1.0 mm thickness, the durability is promising.
- ZLS crowns can exhibit clinically acceptable internal marginal gaps (≤150 μm).
- After the firing process, there is an increase of modulus of elasticity, flexural strength, fracture toughness, hardness, and characteristic strength, in parallel with a decrease of both the Weibull modulus and volume (shrinkage).
- The firing and polishing procedures positively affect the fatigue failure load.
- ZLS seems to show a certain degree of biocompatibility, allowing proliferation, coverage, and spreading of HGFs, encouraging its use in contact with peri-implant soft tissues.

Although ZLS can be considered promising hybrid ceramic materials for CAD-CAM technologies, it cannot be denied that further *in vitro* and, in particular, randomized controlled trials *in vivo* studies are needed to accurately define mechanical properties and biocompatibility of ZLS-based restorations both tooth- and implant-supported.

Declaration of Competing Interest

The authors report no declarations of interest.

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