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Bioactive Composites in Dentistry: A Comparative Study of Tissue Regeneration, Biological Activity, and Clinical Outcomes in Various Dental Applications

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ABSTRACT

Background: Bioactive composites represent a new generation of dental restorative materials that not only restore tooth structure but also actively participate in tissue regeneration and promote biological activity.

Objective: To compare the tissue regenerative potential, biological activity, and clinical outcomes of various bioactive composite materials in various dental applications.

Methods: A comparative cohort study was conducted at the Islam Dental College Sialkot, Pakistan, over 12 months from Jan, 2024 to December, 2024. A total of 144 participants with restorations or periodontal defects were included using consecutive sampling, divided equally between bioactive composite and comparator groups. In vitro assessments included microhardness, hydroxyapatite formation, calcium ion release, and pH changes at baseline, 1, 4, and 12 weeks. Data were analyzed using SPSS 25.0, with significance set at $p \leq 0.05$.

Results: Bioactive composites showed significantly higher microhardness (45.2 ± 5.8 vs. 28.7 ± 4.9 kg/mm²), hydroxyapatite formation (12.5 ± 2.1 vs. 5.8 ± 1.9 µm), calcium ion release (15.8 ± 3.4 vs. 4.2 ± 1.1 ppm), and pH elevation ($p < 0.001$) than comparators. Clinically, restoration retention (95.8% vs. 86.1%), marginal adaptation, periodontal defect fill (3.8 ± 0.6 vs. 2.5 ± 0.7 mm), and healing index scores were superior in the bioactive group, with fewer secondary caries.

Conclusion: Bioactive composites enhance tissue regeneration, biological activity, and clinical performance, supporting their use as a reliable alternative to conventional materials in various dental applications.

Keywords: *Bioactive composites, tissue regeneration, remineralization, clinical outcomes, dental restorative materials*

1. INTRODUCTION

The development of restorative dental materials has evolved remarkably over the past few decades, shifting from passive restorative substances to biologically active materials that interact with surrounding tissues.(1) Traditional resin-based composites, although widely used for their esthetics and mechanical properties, are biologically inert and often fail to stimulate tissue repair or prevent recurrent caries.(2) In contrast, bioactive composites represent a new generation of restorative materials that can actively participate in the remineralization of tooth structure, release therapeutic ions, and promote tissue regeneration at the interface of the restoration. These materials bridge the gap between mechanical durability and biological compatibility, offering the potential for long-term clinical success in restorative dentistry.(1)

Bioactivity in dental materials is primarily defined by their ability to form a hydroxyapatite layer when in contact with physiological fluids, thereby bonding chemically to the tooth and surrounding tissues.(3) Incorporation of components such as bioactive glass, calcium phosphate, and fluoride-releasing agents enhances remineralization and exerts antimicrobial properties, reducing the risk of secondary caries.(4) Recent formulations, such as calcium-silicate-based composites, fluoroaluminosilicate glass-containing composites, and nano-hydroxyapatite-based materials, have demonstrated promising biological interactions with dentin and pulp cells, indicating their potential for regenerative applications.(4)

Globally, dental caries and tooth loss remain highly prevalent conditions, affecting approximately 2.5 billion people according to the Global Burden of Disease (GBD) 2019 report.(5) In Pakistan and other developing nations, the prevalence of dental caries among school-aged children ranges between 60–80%, highlighting the urgent need for restorative materials that not only replace lost tissues but also prevent disease recurrence.(6, 7) Additionally, the aging population and increased demand for esthetic and biologically compatible restorations have driven the clinical adoption of bioactive materials in restorative, endodontic, and periodontal procedures.

While numerous studies have explored the mechanical and esthetic aspects of conventional composites, limited comparative data exist regarding the tissue regenerative potential, biological activity, and clinical performance of different bioactive composite formulations across various dental applications. Understanding these parameters is crucial for optimizing clinical decision-making and material selection in both restorative and regenerative dentistry. Despite growing evidence supporting bioactive materials, the extent to which different bioactive composites promote tissue regeneration and influence clinical outcomes remains underexplored. Comparative analysis of their biological behavior, ion release capacity, and interface integration can provide critical insights into their effectiveness in real-world dental practice. The present study aimed to compare the tissue regenerative potential, biological activity, and clinical outcomes of various bioactive composite materials used in various dental applications.

2. METHODOLOGY

This study employed a comparative cohort design, allowing the evaluation of bioactive composite materials under natural clinical and laboratory conditions. The study was conducted in Islam Dental College Sialkot, Pakistan, over 12 months from Jan, 2024 to December, 2024.

The sample size was calculated using the OpenEpi software (version 3.03). Data from a previous study demonstrated that the remineralization rate of *Activa BioActive Restorative* was approximately 60%**,** compared to 35% for conventional glass ionomer cement in similar experimental conditions. These proportions were entered into OpenEpi with a 95% confidence level, 80% power, and equal group ratio (1:1). The calculated minimum sample size was 60 per group, yielding a total of 120 specimens or participants**.** To compensate for possible dropouts and follow-up losses, the sample size was increased by 20%, resulting in a total of 144 subjects included in the study.

A consecutive sampling technique was used for the clinical part, where eligible patients presenting to the dental outpatient department during the study period were included until the required sample size was achieved. For the in vitro part, purposive sampling was applied to collect extracted human teeth that met the inclusion criteria. Patients between 18 and 60 years of age with restorable dental defects suitable for restoration or with intrabony periodontal defects of ≥3 mm were included. All selected teeth were vital (when applicable), free from abscesses or sinus tracts, and located in patients with no systemic illness known to interfere with healing. Patients with allergies to composite components, non-restorable teeth, advanced root resorption, or those taking medications such as corticosteroids that affect healing were excluded. Pregnant and lactating women were also excluded for ethical reasons. For the in vitro specimens, extracted sound teeth free of cracks, caries, or previous restorations were included, while teeth with extensive decay or structural damage were excluded.

Data collection was carried out in two phases: an in vitro phase and a clinical phase**.** In the in vitro phase, sound extracted teeth were cleaned, standardized in dimension, and artificially demineralized. These were then restored with different bioactive composite materials and comparator materials such as glass ionomer cement or conventional resin composites. Remineralization potential, ion release, and pH changes were assessed at baseline, 1 week, 4 weeks, and 12 weeks using methods such as microhardness testing, scanning electron microscopy (SEM), and energy dispersive X-ray (EDX) analysis. In the clinical phase, participants were treated with one of the bioactive composite materials or comparator materials following standardized restorative or periodontal procedures. Clinical outcomes, including restoration integrity, marginal adaptation, secondary caries development, and periodontal healing parameters, were recorded at baseline, 6 months, and 12 months. The clinicians performing procedures were calibrated before data collection to minimize inter-operator variability, and intra-examiner reliability was assessed using kappa statistics and intraclass correlation coefficients.

The collected data were analyzed using SPSS version 25.0. Continuous variables, such as hardness or mineral gain, were presented as mean ± standard deviation or median (interquartile range), depending on distribution. Categorical variables, such as restoration success or failure, were expressed as frequencies and percentages. Group comparisons were made using the independent sample *t*-test for normally distributed continuous data. Categorical variables were analyzed using chi-square or Fisher's exact test. Within-group comparisons over time were analyzed using paired *t*-tests. A *p*-value ≤0.05 was

considered statistically significant.

3. RESULTS

At baseline, both groups were comparable in terms of demographic and clinical characteristics. The mean age of participants was similar between the bioactive composite group and the comparator group (34.2 ± 10.1 vs. 33.8 ± 9.6 years, p = 0.78). Gender distribution was balanced, with males representing 52.8% of the bioactive group and 50.0% of the comparator group (p = 0.74). Regarding defect type, the majority of participants in both groups presented with Class II restorations (62.5% vs. 65.3%), while the remainder had periodontal intrabony defects, with no statistically significant difference between the groups (p = 0.71). (Table 1).

Table 1. Baseline Demographic and Clinical Characteristics of Participants (n = 144)

Variable	Category	Bioactive Composite (n=72)	Comparator Material (n=72)	p-value
Age (years)	**Mean ± SD**	34.2 ± 10.1	33.8 ± 9.6	0.78
Gender	**Male**	38 (52.8%)	36 (50.0%)	0.74
	Female	34 (47.2%)	36 (50.0%)	
Defect Type	**Class II Restoration**	45 (62.5%)	47 (65.3%)	0.71
	Periodontal Intrabony	27 (37.5%)	25 (34.7%)	

In vitro analysis demonstrated that the bioactive composite exhibited significantly higher tissue regenerative potential and biological activity compared to the comparator material. Microhardness increased markedly in the bioactive group (45.2 ± 5.8 kg/mm²) versus the comparator (28.7 ± 4.9 kg/mm², p < 0.001), indicating superior remineralization. Similarly, hydroxyapatite formation was greater in the bioactive composite (12.5 ± 2.1 µm) than in the comparator (5.8 ± 1.9 µm, p < 0.001). Ion release over four weeks was substantially higher for the bioactive material (15.8 ± 3.4 ppm vs. 4.2 ± 1.1 ppm, p < 0.001), and the pH of the surrounding medium increased more in the bioactive group (7.9 ± 0.3 vs. 6.8 ± 0.4, p < 0.001), reflecting enhanced bioactivity and a favorable environment for tissue regeneration. (Table 2).

Table 2. In Vitro Tissue Regeneration and Biological Activity

Parameter	Bioactive Composite (Mean ± SD)	Comparator Material (Mean ± SD)	p-value
Microhardness Increase (Knoop Hardness, kg/mm²)	45.2 ± 5.8	28.7 ± 4.9	<0.001*
Hydroxyapatite Formation (µm, SEM-EDX)	12.5 ± 2.1	5.8 ± 1.9	<0.001*
Ion Release (Ca^{2+}, ppm, 4 weeks)	15.8 ± 3.4	4.2 ± 1.1	<0.001*
pH Increase (in artificial saliva, baseline to 4 weeks)	7.9 ± 0.3	6.8 ± 0.4	<0.001*
**Statistically significant*			

At 12 months follow-up, clinical outcomes favored the bioactive composite group. Restoration retention was higher in the bioactive group (95.8%) compared to the comparator (86.1%, p = 0.04), and excellent marginal adaptation was observed more frequently (88.9% vs. 73.6%, p = 0.02). The incidence of secondary caries was lower with the bioactive composite (2.8% vs. 11.1%, p = 0.04). Periodontal defect fill was significantly greater in the bioactive group (3.8 ± 0.6 mm) than in the comparator group (2.5 ± 0.7 mm, p < 0.001), and a higher proportion of sites achieved a healing index score ≥8 (84.7% vs. 66.7%, p = 0.01), demonstrating superior regenerative and clinical performance. (Table 3).

Table 3. Clinical Outcomes at 12 Months Follow-Up

Outcome	Bioactive Composite (n=72)	Comparator Material (n=72)	p-value
Restoration Retention	69 (95.8%)	62 (86.1%)	0.04*
Marginal Adaptation Excellent	64 (88.9%)	53 (73.6%)	0.02*
Secondary Caries	2 (2.8%)	8 (11.1%)	0.04*
Periodontal Defect Fill (mm, mean ± SD)	3.8 ± 0.6	2.5 ± 0.7	<0.001*
Healing Index Score ≥8	61 (84.7%)	48 (66.7%)	0.01*
**Statistically significant*			

The temporal analysis of ion release and pH changes demonstrated that the bioactive composite consistently exhibited higher calcium ion release and greater alkalization of the surrounding medium compared to the comparator material. At baseline, both groups had similar calcium levels and pH (Ca^{2+}: 0.5 ± 0.2 vs. 0.4 ± 0.1 ppm; pH: 6.9 ± 0.2 for both). By 1 week, calcium release in the bioactive group increased substantially to 6.8 ± 1.5 ppm, compared to 1.2 ± 0.3 ppm in the comparator, with a corresponding rise in pH to 7.5 ± 0.3. At 4 weeks, the bioactive composite maintained elevated ion release (15.8 ± 3.4 ppm) and higher pH (7.9 ± 0.3) relative to the comparator (4.2 ± 1.1 ppm; pH 6.8 ± 0.4). By 12 weeks, the bioactive group continued to demonstrate superior calcium release (17.5 ± 3.9 ppm) and pH elevation (8.0 ± 0.2), reflecting sustained bioactivity and a favorable environment for remineralization and tissue regeneration. (Table 4).

Table 4. Comparative Ion Release and pH Changes over Time (Bioactive Composite vs Comparator).

Time Point	Ca^{2+} Release (ppm) Bioactive	Ca^{2+} Release (ppm) Comparator	pH Bioactive	pH Comparator
Baseline	0.5 ± 0.2	0.4 ± 0.1	6.9 ± 0.2	6.9 ± 0.2
1 week	6.8 ± 1.5	1.2 ± 0.3	7.5 ± 0.3	6.9 ± 0.2
4 weeks	15.8 ± 3.4	4.2 ± 1.1	7.9 ± 0.3	6.8 ± 0.4
12 weeks	17.5 ± 3.9	5.0 ± 1.4	8.0 ± 0.2	6.9 ± 0.3

4. DISCUSSION

This research examined the capacity of bioactive composites for use in dentistry based on tissue regeneration, biological activity, and clinical performance. The findings present both agreement and further text to current literature. The study showed significant increases in microhardness, hydroxyapatite formation, calcium ion release, and pH increase when using bioactive composites in comparison to traditional restoratives. This aligns with Bhatia et al. (2022), who also demonstrated elevated calcium ion release and shear bond strength with bioactive composites, compared to resin-modified glass ionomers in the restoration of primary teeth.(8) In a similar vein, a study conducted by Ahmad et al. (2025) showed that bioactive composites promoted ion exchange in leathery dentine remnants, which enhanced remineralization. .(9)

rom a clinical standpoint, the present study showed that the bioactive composite group had a higher restoration retention rate, marginal adaptation, lower incidence of secondary caries, and improved healing in the periodontal tissue in comparison to the non-bioactive group. These improved outcomes are consistent with work performed by Ebrahim et al. (2025), which showed that bioactive bulk-fill composites had better clinical performance over a year in patients receiving head and neck radiation.(10) Also, a systematic review by de Carvalho et al. (2024) noted that bioactive resin materials were found to perform in as good clinical fashion as conventional composites in caries prevention and in extending the longevity of direct posterior restorations.(11)

The results of our study for sustained calcium ion release and pH raise in bioactive composites support the findings of Venkataiah et al. (2025), who examined ion release behavior of a bioactive resin cement in varying pH environments and showed sustained ion release across different pH levels.(12) In addition, research by Aliberti et al. (2025) pointed out that the bioactive restorative materials released and recharged ionic components in response to pH changes, which allowed continuous ion exchange with oral fluids.(13)

We also found support for our results from comparative evaluations. For instance, the research of El-Salamouny et al. (2025) compared clinical performance of Cention N, a novel alkasite bioactive restorative material, to other traditional materials, reporting that Cention N performed equally or better with respect to restoration longevity and secondary caries prevention.(14) Furthermore, Ferracane (2023) reviewed dental materials' bioactivity and identified that ion release and pH

increase should enhance the restorative effect.(3)

This study holds potentially significant clinical implications for restorative and regenerative dentistry. Biologically active composites do more than restore tooth structure; they promote remineralization and promote tissue regenerative properties to minimize risk for secondary caries while providing benefits for enhancement of periodontal healing. Sustained ion release, along with long-lasting pH changes, provide a biologically considerate environment that enhances patient care, particularly for patients with high caries risk or impaired periodontal care. Clinicians may want to consider the usefulness of these biologically active materials as a sound substitute for traditional composites towards long-term restorative success with minimized retreatment and patient benefits.

5. LIMITATIONS

Although this study produced encouraging results, it had certain limitations. Firstly, the size of the sample in this study (clinical study report) was sufficient for statistical analysis, but it was based on a single center, which may limit the generalizability of the findings to wider populations. Secondly, having a 12-month follow-up established a baseline to evaluate short-term clinical performance; however, this timeframe may not reflect long-term clinical outcomes such as restoration longevity, late secondary caries, or late-radiological assessments. Thirdly, in vitro assessments provided some understanding of biological activity and tissue regeneration, but it may not be an exact surrogate for a complex oral environment. It should be noted that operator-dependent variability and patient-specific factors, such as oral hygiene and diet, may have affected clinical outcomes, although protocols were calibrated and standardized.

6. CONCLUSION

Bioactive composites exhibited better tissue regenerative capability, greater biological activity, and a higher level of clinical performance than traditional restorative materials. Moreover, materials released ions over a period of time (10-day interval), facilitated remineralization, and enhanced retention of the restorations, marginal adaptation of the restorations, and healing of the periodontal tissues. Based on these results, bioactive composites should be viewed as a viable alternative to traditional restorative, endodontic, and periodontal materials, especially considering that bioactive materials promote tissue regeneration and are suitable for long-term clinical performance.

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