Hydrophilic Properties of Dental Implant Surfaces: Literature Review

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Abstract: This literature review investigated the role of implant surface wettability in the success of dental implants, focusing on hydrophilic properties. Thorough search of PubMed, EBSCO, MDPI, and Google Scholar was conducted from November 11 to December 16, 2024, using terms related to implant surface wettability, hydrophilicity, immune cells, soft tissues and osseointegration. Studies published in English, focusing on the hydrophilicity of dental implants, were included. Exclusion criteria applied to studies unrelated to wettability or non-English articles. From 33 initial studies, 28 met inclusion criteria, with 15 undergoing full-text analysis and 13 reviewed from abstracts. Furthermore, each article went through quality analysis using CONSORT checklist designed for dental materials research and new techniques. Hydrophilic surfaces have been shown to enhance early cell adhesion, proliferation, and differentiation, particularly in osteoblastic activity, which is essential for osseointegration. In addition to promoting bone healing, hydrophilic surfaces also support soft tissue integration, improving the formation of a tight epithelial seal and reducing the risk of infection and periimplantitis. The response of innate immune cells, such as neutrophils and macrophages, is also influenced by surface wettability, with hydrophilic surfaces fostering an environment conducive to bone formation by promoting beneficial immune cell activity and osteogenesis. This review highlights the importance of surface modification, specifically hydrophilic treatments, in optimizing the biological response and long-term success of dental implants.

Keywords: Contact angle, Dental implants, Epithelial cells, Hydrophilicity, Immune cells, Osseointegration, Wettability.

1. INTRODUCTION

Successful dental implant therapy is affected by both the dental implant characteristics such as implant surface wettability and roughness and by the patient tissue and immune response to the implant. Most studies have found that dental implant surfaces with low contact angle (CA), described as hydrophilic, tend to enhance the initial stages of cell adhesion, proliferation, differentiation and bone osseointegration compared to hydrophobic dental implant surfaces with high CA [1].

Wettability is typically measured by the CA, defined as the angle formed between the tangent line to the surface of a liquid drop at the three-phase boundary and the horizontal solid surface. In our case, the apical portion of the dental implant. In a recent overview, it was reported that five distinct types of implant surface treatments had been documented, these surfaces were turned (machined), titanium plasma sprayed (TPS), blasted, sandblasted and acid-etched (SLA) and anodized ones [2, 3]. All aforementioned treatments are affecting the wettability degree of the dental implant. Wettability of dental implant is classified in to four groups being super-hydrophilic (0° -50°), hydrophilic (50°-90°), hydrophobic (90°-150°) and super-hydrophobic (150°-180°) depending on the CA [4].

Brånemark discovered direct bone anchorage of metallic implants in 1962, with clinical application for dental implants beginning in 1965. He coined the term "osseointegration" in 1976, defining it as direct contact between implants and bone at the light microscope level [5]. The processes of osseointegration involve an initial connection between alveolar bone and the implant, and later, biological fixation through continuous bone arrangement and remodeling toward and from the implant, distance osteogenesis and contact osteogenesis, respectively [6].

To prevent bacteria from affecting healing or implant performance, it is important to create a strong, lasting barrier to protect the peri-implant surrounding structures with the help of soft tissue cells, like keratinocytes and fibroblasts. After the placement of the implant, connective tissue wound healing progresses through several key stages: the formation and attachment of a fibrin clot to the implant surface, the deposition of extracellular matrix (ECM) proteins followed by the recruitment of connective tissue cells, the conversion of the clot into granulation tissue, and the migration of epithelial cells over the fibrin clot and

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granulation tissue. To optimize this aspect, the surface wettability of the implant is crucial [7].

Osteoimmunology examines the connection between bone tissue metabolism and the immune system. After a dental implant is placed, innate immune cells, including neutrophils and macrophages, gather at the implantation site and secrete pro-inflammatory cytokines, chemokines, and growth factors that influence osteoprogenitor cells [6, 8-10].

This review will give an insight into the importance of bone formation, soft tissue integration and immune cell migration in relation to dental implant surface energy.

2. MATERIALS AND METHODS

2.1. Protocol Registration and Review Reporting

This review does not have a registered protocol. It follows a structured literature review approach designed to ensure comprehensive and transparent coverage of the topic.

2.2. Inclusion and Exclusion Criteria

This paper explored the subject "wettability property of dental implants" through a literature review and qualitative approach. The main goal of this paper was to gather data and help to understand the benefits of hydrophilic dental implants on the outcome.

Inclusion criteria included studies related to the topic of hydrophilicity of dental implants, immunity and osseointegration and published in English. Exclusion criteria included papers that did not focus on the wettability of dental implants or were not written in English.

2.3. Search Methods for Identification of Studies

2.3.1. Information Sources

A thorough search was undertaken to identify and analyze articles relevant to this literature review. The databases used included PubMed, EBSCO, MDPI and Google Scholar. The initial search was conducted on November 11, 2024, and updates were performed on November 28, 2024, December 12, 2024, and December 16, 2024.

2.3.2. Search Terms

Papers regarding the topic were searched from legitimate sources such as PUBMED, EBSCO, MDPI and Google Scholar. Publications back from 1977 up to 2024 in the English language were collected. Used search terms can be found below in Table **1**.

2.3.3. Selection Criteria

The titles of the initially retrieved studies were reviewed, followed by a manual search. After removing irrelevant titles, the abstracts were assessed, and those meeting the inclusion criteria were included. Full-text reviews were conducted for the selected studies or when abstracts lacked sufficient information. In some cases, full-text versions of potentially relevant studies were inaccessible through institutional subscriptions or journal access limitations. Therefore, 13 studies were included based on information available in their abstracts. These abstracts provided sufficient methodological and outcome data related to the topic. While inclusion based solely on abstracts may introduce a potential source of selection bias due to limited detail and the inability to fully assess study quality, these entries were retained to ensure a comprehensive overview of available evidence within the defined topic scope.

2.3.4. Data Extraction

During database screening, 28 publications were accepted. Data from the selected publications were extracted manually by two independent reviewers. The extracted information included: author and year of publication, study design (*in vitro*, *in vivo*, or clinical), biological outcome assessed (osseointegration, soft tissue integration, or immune response), and main findings related to surface hydrophilicity. Any discrepancies between reviewers were resolved through discussion.

2.4. Quality Analysis

The quality of the included studies was evaluated using a modified CONSORT (CONsolidated Standards

Table 1: Search Terms for Literature Search

Search Engine	Search Term
PubMed	"Hydrophilicity of dental implants," "Osseointegration," "Cellular response to dental implant."
EBSCO	"Hydrophilicity of dental implants," "Osseointegration," "Cellular response to dental implant."
Google Scholar	"Hydrophilicity of dental implants," "Osseointegration," "Cellular response to dental implant."
MDPI	"Hydrophilicity of dental implants," "Osseointegration," "Cellular response to dental implant."

Of Reporting Trials) checklist designed for dental materials research and new techniques. The checklist includes 14 points across 15 items (with item 2 divided into 2a and 2b) to assess the quality of information in an article's abstract, introduction, methods, results, discussion, and supplementary sections.

The evaluation process (Table **2**):

- YES (+): Item met the criteria.
- NO (-): Item did not meet the criteria.

Studies were categorized by the percentage of fulfilled items and associated risk of bias:

1. ≥70%: Low risk.
2. 50–69%: Moderate risk.
3. ≤49%: High risk.

2.5. Data Synthesis

Due to methodological diversity among the studies, a narrative synthesis was performed. The results were organized into three main thematic categories: osseointegration, soft tissue integration, and immune response.

3. RESULTS

A total of 33 relevant publications were initially identified through electronic database searches (Table 1). After applying the inclusion and exclusion criteria, four articles were excluded due to their non-compliance with the criteria, and one was removed due to duplication. This process left 28 articles for further evaluation. Among these 28 articles, 15 underwent a detailed full-text analysis, while the remaining 13 were analyzed based solely on their abstracts (Table **3**).

Table 2: Quality Assessment and Risk of Bias Evaluation Following the CONSORT Checklist

Study	1	2a	2b	3	4	5	6	7	8	9	10	11	12	13	14	Risk of bias
Eriksson *et al*. (2004)	+	+	+	+	+	+	-	-	-	-	+	+	+	+	-	66.67%
Wennerberg *et al*. (2018)	+	+	+	+	+	-	+	-	-	-	+	+	+	+	-	66.67%
Bornstein *et al*. (2008)	+	+	+	+	+	+	-	-	+	-	+	+	+	+	-	73.34%
Gittens *et al*. (2014)	-	+	+	-	+	-	-	-	-	-	+	-	+	+	+	46.67%
Brånemark *et al*. (1977)	-	+	+	+	+	-	-	-	-	-	+	+	+	-	+	53.34%
Kondo *et al*. (2024)	+	+	+	-	+	-	-	-	-	-	+	+	+	+	+	60%
Rompen *et al*. (2006)	+	+	+	+	+	-	-	-	-	-	+	+	+	-	-	53.34%
MacLeod *et al*. (2006)	+	+	+	+	+	-	-	-	-	-	+	+	+	+	+	66.67%
Mello-Machado *et al*. (2021)	+	+	+	+	+	+	+	-	-	-	-	+	+	+	+	73.34%
Amengual-Peñafiel *et al*. (2021)	+	+	+	-	-	-	-	-	-	-	-	+	+	-	-	33.34%
Grandin *et al*. (2012)	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100%
Rack *et al*. (2006	+	+	+	+	+	-	-	-	-	-	+	+	+	-	+	60%
Albrektsson *et al*. (2017)	+	+	+	-	-	-	-	-	-	-	-	+	+	-	-	33.34%
Hicklin *et al*. (2016)	+	+	+	+	-	+	+	+	+	-	+	+	-	+	+	80%
Zhao *et al*. (2005)	+	+	+	+	+	-	-	-	-	-	+	+	+	-	-	53.34%
Presland *et al*. (2000)	+	+	+	-	-	-	-	-	-	-	-	-	-	-	+	26.67%
Quirynen *et al*. (2002)	+	+	+	+	-	-	-	-	-	-	+	+	-	-	-	40%
Esposito *et al*. (1999)	+	+	+	+	+	+	+	+	+	+	-	-	-	-	+	73.34%
Abaricia *et al*. (2021)	+	+	+	+	-	-	-	-	-	-	+	+	+	+	+	60%
Croes *et al*. (2015)	+	+	+	+	+	+	-	-	-	-	+	+	-	+	-	60%
Bastian *et al*. (2016)	+	+	+	+	-	-	-	-	-	-	+	+	+	+	+	60%
Glass *et al*. (2011)	-	+	+	+	+	+	-	-	-	-	+	+	+	+	+	66.67%
Hazeldine *et al*. (2014)	+	+	+	+	-	-	-	-	-	-	-	+	+	+	+	53.34%
Abaricia *et al*. (2020)	+	+	+	+	-	-	-	-	-	+	+	+	+	+	+	66.67%
Wu *et al*. (2013)	+	+	+	+	-	-	-	-	-	+	+	+	+	+	-	66.67%
Loi *et al*. (2016)	-	+	+	+	+	+	-	-	-	+	+	+	-	+	-	60%
Lu *et al*. (2017)	+	+	+	+	+	+	-	-	-	+	+	+	-	+	+	73.34
Hamlet *et al*. (2019)	+	+	+	+	+	-	-	-	-	-	+	+	+	+	-	60%

Table 3: Included Study Characteristics

Author (Year)	Database Search	Conclusion
Eriksson *et al*. (2004)	PubMed	"Dental implant surfaces with low contact angle, described as hydrophilic, tend to enhance the early stages of cell adhesion, proliferation, differentiation and bone osse-ointegration compared to hydrophobic dental implant surfaces with high contact angle." "Hydrophilicity had a greater role in the early stages promoting osteoblastic differentiation" "The influence of implant surface wettability transcends its role at the protein and cellular level and has been confirmed *in vivo* and in the clinic."
Wennerberg *et al*. (2018)	PubMed	"Five different types of implant surface treatments have been documented for more than years."
Bornstein *et al*. (2008)	PubMed	"Five different types of implant surface treatments have been documented for more than years."
Gittens *et al*. (2014)	Google Scholar	"Wettability of dental implant is classified in to four groups being super-hydrophilic, hydrophilic, hydrophobic and super-hydrophobic depending on the contact angle."
		"Higher keratinocyte proliferation on super-hydrophilic surfaces resulted in faster surface coverage, suggesting that implants with super-hydrophilic surface could lead to faster restoration of a tight epithelial seal."
Brånemark *et al*. (1977)	PubMed	"Osseointegration coined as a term- direct contact between implants and bone at the light microscope."
Kondo *et al*. (2024)	PubMed	"The processes of osseointegration involve an initial connection between alveolar bone and the implant, and later, biological fixation through continuous bone arrangement and remodeling toward and from the implant, distance osteogenesis and contact osteogenesis respectively."
Rompen *et al*. (2006)	PubMed	"The response of soft tissue cells, like keratinocytes and fibroblasts, to implant surface wettability is critical for long-term success". "Intimate integration of soft tissue cells with the implant is required to seal the implantation site from the external environment, avoiding infections and periimplantitis, and ensuring a successful outcome", "After installation of the transmucosal component, the healing of the connective tissue wound involves distinct processes: formation and (hopefully) adhesion of a fibrin clot to the implant surface, adsorption of extra cellular matrix proteins and subsequently of connective tissue cells to the implant surface, transformation of the clot into granulation tissue, migration of epithelial cells on top of the fibrin clot/granulation tissue".
MacLeod *et al*. (2006)	PubMed	"Neutrophils and macrophages play a key role in wound healing. When an implant is placed, these cells quickly gather at the site, releasing inflammatory mediators that influence the recruitment, growth, and differentiation of osteoprogenitor cells for osseointegration."
Mello-Machado *et al*. (2021)	Google scholar	"Neutrophils and macrophages play a key role in wound healing. When an implant is placed, these cells quickly gather at the site, releasing inflammatory mediators that influence the recruitment, growth, and differentiation of osteoprogenitor cells for osseointegration."
Amengual-Peñafiel *et al*. (2021)	EBSCO	"Neutrophils and macrophages play a key role in wound healing. When an implant is placed, these cells quickly gather at the site, releasing inflammatory mediators that influence the recruitment, growth, and differentiation of osteoprogenitor cells for osseointegration. "Macrophages and neutrophils participate in osseointegration by releasing inflammatory mediators that affect the recruitment, proliferation, and differentiation of osteoprogenitor cells."
Grandin *et al*. (2012)	MDPI	"For dental implant applications, titanium and its alloys, including commercially pure, titanium –aluminum-vanadium and, more recently, titanium-zirconium, are used due to their favorable weight-to-strength ratio, good biological performance, and adequate corrosion resistance under normal conditions."
Rack *et al*. (2006)	Google Scholar	"For dental implant applications, titanium and its alloys, including commercially pure, titanium –aluminum-vanadium and, more recently, titanium-zirconium, are used due to their favorable weight-to-strength ratio, good biological performance, and adequate corrosion resistance under normal conditions."
Albrektsson *et al*. (2017)	Google Scholar	"Osseointegration has a novel definition: osseointegration is a foreign body reaction where interfacial bone is formed as a defense reaction to shield off the implant from the tissues."
Hicklin *et al*. (2016)	PubMed	"Implants with a hydrophilic, moderately rough endosseal surface 3 weeks after placement appears to be a safe and predictable treatment option in healed sites in the posterior mandible without need of bone augmentation procedures".
Zhao *et al*. (2005)	PubMed	"Hydrophilic surfaces have been shown to enhance osteoblast maturation; production of local factors and mineralization compared to hydrophobic surfaces."
Presland *et al*. (2000)	Google scholar	"Intimate integration of soft tissue cells with the implant is required to seal the implantation site from the external environment, avoiding infections and periimplantitis, and ensuring a successful outcome."
Quirynen *et al*. (2002)	EBSCO	"Intimate integration of soft tissue cells with the implant is required to seal the implantation site from the external environment, avoiding infections and periimplantitis, and ensuring a successful outcome."

Rolando *et al*. (2014)	PubMed	"Higher keratinocyte proliferation on super-hydrophilic surfaces resulted in faster surface coverage, suggesting that implants with super-hydrophilic surface could lead to faster restoration of a tight epithelial seal."
Esposito *et al*. (1999)	PubMed	"The failure of dental implant is often due to impaired bone healing after implant placement, owing to the formation of fibrous scar tissue between the implant surface and the surrounding bone during the initial phase."
Abaricia *et al*. (2021)	EBSCO	"Macrophages and neutrophils participate in osseointegration by releasing inflammatory mediators that affect the recruitment, proliferation, and differentiation of osteoprogenitor cells."
Croes *et al*. (2015)	PubMed	"TNF*-α, interleukin IL**-6, and IL-17, have been shown to promote the proliferation and osteogenic differentiation of MSCs+ or pre-osteoblast cells".
Bastian *et al*. (2016)	PubMed	"Neutrophils produce fibronectin within the hematoma of human wounds, and stromal cells, which gather within the fibronectin scaffold, produce type I collagen to promote bone formation."
Glass *et al*. (2011)	PubMed	"A high dose of TNF-α, exhibit an inhibitory effect on the osteogenesis of MSCs."
Hazeldine *et al*. (2014)	Google scholar	"Over-migration of neutrophils can produce excessive amounts of cytokines and induce massive NET++ formation, thereby accelerating tissue damage and harming nearby healthy tissues."
Abaricia *et al*. (2020)	PubMed	"Neutrophils cultured on micro-rough hydrophilic titanium discs showed significantly lower production of pro-inflammatory mediators and decreased NET formation compared with those cultured on micro-rough titanium discs."
Wu *et al*. (2013)	PubMed	"M1 macrophages contribute to the clearance of debris at the injured site, whereas M2 macrophages promote MSC- mediated bone formation by secreting mediators in later stages".
Loi *et al*. (2016)	PubMed	"M2 macrophages have been found to release IL-4 and contain bone morphogenetic protein-2".
Lu *et al*. (2017)	PubMed	"M2 macrophages have been found to release IL-4 and contain bone morphogenetic protein-2".
Hamlet *et al*. (2019)	PubMed	"Macrophages polarized to the M2 phenotype by a hydrophilic micro-rough titanium surface can promote osteoprogenitor cell differentiation".

*Tumor necrosis factor; **Interleukin; +Mesenchymal stem cells; ++ Neutrophil extracellular traps.

Osseointegration

Eriksson *et al*. demonstrated that hydrophilic surfaces accelerate early-stage bone formation through increased production of osteogenic markers [1]. Furthermore, Zhao *et al*. reported that mineralization and cellular maturation processes were more efficient on hydrophilic surfaces compared to hydrophobic ones [11]. Clinical trials by Hicklin *et al*. confirmed these findings, demonstrating that implants with hydrophilic surfaces achieved successful osseointegration even under early functional loading conditions [12]. These results emphasized the importance of hydrophilic modifications in achieving favorable biological responses.

Soft tissue integration

Soft tissue integration was another critical aspect where hydrophilic surfaces excel. Studies by Rompen ***et al***. highlighted that hydrophilic surfaces promote the proliferation of keratinocytes and fibroblasts, key cell types involved in forming a strong epithelial seal that minimizes the risk of bacterial invasion and peri-implantitis [7]. Additionally, the extracellular matrix production supported by fibroblasts on hydrophilic surfaces further strengthened soft tissue attachment [4].

Immune response

Abaricia *et al*. demonstrated that neutrophils on hydrophilic titanium surfaces exhibit reduced production of pro-inflammatory mediators like TNF-α and IL-6, creating less inflammatory and more osteogenic properties [13]. Moreover, these surfaces encourage macrophage polarization toward the M2 phenotype, associated with regenerative functions, as shown by Lu *et al*. and Hamlet *et al*. [14, 15]. Hydrophilic treatments were essential for enhancing immune responses and thus the implant longevity.

The review identified hydrophilic surface treatments as a crucial factor in improving dental implant outcomes. These modifications positively influence the early-stage bone formation, strengthen soft tissue attachment, and regulate immune responses to promote healing.

4. DISCUSSION

For dental implant applications, titanium (Ti) and its alloys, including commercially pure (cp) Ti, titanium –aluminum-vanadium (Ti6Al4V) and, more recently, titanium-zirconium (TiZr), are selected for their favorable weight-to-strength ratio, excellent biological performance, and adequate corrosion resistance under normal conditions [16, 17].

Osseointegration is described as: “a foreign body reaction where interfacial bone is formed as a defense reaction to shield off the implant from the tissues” [18]. The first step is the formation of blood clots on the implant surface which is followed by fibrous ossification and lamellar bone formation. Secondly, mesenchymal stem cells (MSCs) and osteoblasts arrive at the site of implantation. Exposure of MSCs to inflammatory cytokines and growth factors causes osteoblast differentiation of MSCs and as subsequent osteoblast proliferation [4]. There are two types of bone formation in osseointegration, one being contact osteogenesis, osteoblasts deposit bone matrix directly onto the implant surface, and the second being distance osteogenesis where bone matrix is deposited by osteoblasts on the bone edge surrounding the implant [6]. Several studies have investigated the role of hydrophilic titanium surfaces in promoting osseointegration, all highlighting their positive effects. Eriksson *et al*. demonstrated that hydrophilic surfaces led to faster cellular activation and greater osteoblastic differentiation, with increased vascular endothelial growth factor (VEGF), osteocalcin, and alkaline phosphatase positive cells after 21 days [1]. This aligns with Zhao *et al*. [11], who found that hydrophilic surfaces enhance osteoblast maturation, mineralization, and the production of local factors. These findings are consistent with the work of Hicklin *et al*. [12], who showed that hydrophilic, moderately rough titanium surfaces supported osteoblastic differentiation, contributing to successful osseointegration when functional occlusal loading was applied three weeks after implant placement. However, there are differences in the methodologies and scope of these studies. Eriksson *et al*. [1] focused on early-stage cellular responses in animal models, but the small sample size and use of rat tibiae limit the direct applicability to human clinical settings. In contrast, Hicklin *et al*. [12] demonstrated clinical success in human patients but lacked insights into how hydrophilic surfaces influence osteogenesis at the cellular level. Zhao *et al*. [11] offered valuable insights but did not consider the long-term effects or the role of functional loading, which may influence osseointegration in “real-world” applications.

Another key factor influencing the success of dental implants are soft tissue cells and proteins adsorption to the implant surface. The effect of implant surface wettability goes beyond its role at the protein and cellular level and has also been confirmed *in vivo* [1]. In the oral mucosa, keratinocytes are the primary cells of the stratified squamous epithelial layer, while fibroblasts are responsible for producing the supportive extracellular matrix found in the lamina propria, the connective tissue layer beneath the epithelial layer. A strong interconnection between these two layers of soft tissue cells and the implant is essential to seal the implantation site from the external environment of the oral cavity, which is abundant with opportunistic pathogens. This connection helps prevent infections and peri-implantitis, thereby contributing to a successful outcome [7, 19, 20]. Higher keratinocyte proliferation on super-hydrophilic surfaces resulted in faster surface coverage, suggesting that implants with super-hydrophilic surface could lead to faster creation of a tight epithelial seal. However, other studies have found that high surface energies may promote cell adhesion but impair cell motility and subsequent cell functions [4]. Esposito *et al.* [21] suggested that the frequent failure of dental implants is primarily due to inadequate osseointegration following implant placement, which is often a result of fibrous scar tissue forming between the implant surface and the surrounding bone. The discrepancy in findings may be attributed to differences in study methodologies, such as the use of animal models versus clinical trials, and varying implant surface treatments. For instance, Gittens *et al*. [4] focused on cell behavior *in vitro*, which does not fully capture the complex interactions that occur *in vivo*. Furthermore, Esposito *et al*. [21] clinical observations, while highly relevant, do not provide insight into the underlying cellular mechanisms driving the observed outcomes. Future studies should address this inconsistency by using more robust animal models and clinical trials with long-term follow-ups to assess the real-world effectiveness of different surface modifications on osseointegration and soft tissue healing.

Innate immune cells play a crucial role in the survival rate of dental implants, particularly during the wound healing process. Neutrophils and macrophages migrate to the implantation site and contribute to osseointegration by releasing inflammatory mediators that influence the recruitment, proliferation, and differentiation of osteoprogenitor cells [10, 13]. Studies done by Croes *et al.* [22] and Glass *et al.* [23] agreed on the essential involvement of neutrophils in facilitating osteogenesis for successful integration with the alveolar bone. However, differences arise in the roles of pro-inflammatory cytokines, particularly TNF-α, IL-6, and IL-17, with some studies highlighting their ability to enhance osteogenesis, while others suggest that excessive levels of TNF-α inhibit MSC osteogenesis Esposito *et al*. [21] suggested that too much TNF-α can impede osteogenic differentiation, which may disturb successful osseointegration. In one study, within three days of implantation, neutrophils produced fibronectin within the hematoma. This

fibronectin scaffold attracted stromal cells to produce type I collagen and support osteogenesis [24]. This aligns with the general finding that neutrophils are key to osteogenesis but introduces a detailed view regarding their pro-inflammatory role. However, there are discrepancies in terms of the cytokines produced by neutrophils. While some studies focus on osteogenic potential, others warn of the negative effects of excessive cytokine release that can lead to tissue damage through the formation of neutrophil extracellular traps (NET) [25]. Abaricia *et al.* [26] conducted a study focusing on the influence of surface properties on neutrophil activity. They found that neutrophils cultured on micro-rough hydrophilic titanium discs produced significantly lower levels of pro-inflammatory mediators, including TNF-α, IL-6, and IL-17, with reduced NET formation compared to neutrophils on hydrophobic titanium discs. This study shows agreement with the idea that hydrophilic surfaces can mitigate adverse neutrophil activity. However, a limitation of the study is that it does not provide long-term observations to assess the full impact on osseointegration beyond the initial inflammatory phase. Regarding macrophages, studies agree that M1 and M2 macrophages play important roles in the success of implant integration. M1 macrophages assist in debris clearance, while M2 macrophages promote MSC-mediated bone formation by releasing specific mediators such as IL-4 and bone morphogenetic protein 2 (BMP2), which are potent osteoinductive cytokines [14, 27, 28]. The influence of surface properties on macrophage polarization is well-documented, with hydrophilic micro-rough titanium surfaces encouraging M2 polarization, which favors osteoblast differentiation, compared to the M1 polarization seen with hydrophobic surfaces. This is supported by Hamlet *et al*. which suggested that hydrophilic surfaces are beneficial for enhancing osseointegration through improved macrophage functionality [15].

The collective evidence indicates that hydrophilic implant surfaces enhance clinical outcomes through the combined effects of improved osteogenesis, soft tissue sealing, and immune modulation. Increased surface energy accelerates early osteoblast attachment and matrix mineralization [1, 11, 12], while also promoting faster epithelial coverage and fibroblast adhesion, resulting in a more stable biological seal [4, 7, 19]. At the same time, hydrophilic surfaces reduce pro-inflammatory activity of neutrophils and promote regenerative M2 macrophage polarization, creating an immune environment that favors bone formation [13-15]. These interconnected effects act synergistically to improve implant stability and reduce the risk of peri-implant inflammation.

While the existing research provides valuable insights, several gaps remain to be addressed in future studies. The long-term effects of surface modifications on osseointegration and soft-tissue healing are still not fully understood. The development of implants that not only enhance bone integration but also regulate immune responses will be crucial for achieving an optimal balance between inflammation and healing. The included studies vary in design and are mostly based on *in vitro* or animal models, providing limited long-term data and few insights from alternative materials. Hydrophilic implant surfaces should be prioritized in clinical practice for improved osseointegration, especially in patients with healing challenges. Policies should encourage standardized protocols and large clinical trials, while future research should focus on long-term outcomes, new biomaterials, and consistent wettability evaluation methods.

5. CONCLUSIONS

This literature review explored the significance of implant surface wettability, particularly hydrophilic properties, in enhancing the success of dental implants. Hydrophilic surfaces have shown to improve early cellular responses such as adhesion, proliferation, and differentiation, which are critical for osseointegration and bone healing. Moreover, the favorable interaction between soft tissue cells, including keratinocytes and fibroblasts, with hydrophilic surfaces contributes to faster epithelial sealing and reduced risk of infection. Immune cells, particularly neutrophils and macrophages, also play a vital role in the healing process, with hydrophilic surfaces promoting beneficial immune cell activity and improving bone formation.

AUTHOR CONTRIBUTIONS

Conceptualization, Y.R. and D.G.; methodology, Y.R.; software, T.B.; validation, D.G., T.B. and L.M.; formal analysis, B.B.; investigation, Y.R.; resources, T.Č.; data curation, T.Č.; writing—original draft preparation, Y.R.; writing—review and editing, D.G.; visualization, L.M.; supervision, T.B.; project administration, B.B.; funding acquisition, D.G. All authors have read and agreed to the published version of the manuscript.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

ABBREVIATIONS

The following abbreviations are used in this manuscript:

IL Interleukin

TNF Tumor necrosis factor

MSC Mesenchymal stem cells

NET Neutrophil extracellular traps

VEGF Vascular endothelial growth factor

BMP Bone morphogenetic factor

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