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Graphene and Its Derivatives in Dental Implants: A Patent Landscape Study †

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Abstract: Carbon allotropes, including graphene, graphene oxide (GO) and reduced graphene oxide (r-GO), have the potential as coating nanomaterials to improve the performance of dental implants. Furthermore, graphene has demonstrated strong antibacterial activity and enhanced biocompatibility in comparison to other types of carbon nanoscale structures. Several bibliometric studies have been published on the use of graphene-based materials, but they only focus on scientific articles and not patents. Few articles report on a patent study of dental implants, but without focusing on carbon allotropes. The objective of this study is to provide a patent landscape analysis of graphene and its derivatives in relation to dental implants. The search for relevant information was conducted on Espacenet.

Keywords: dental implants; graphene; graphene oxide (GO); reduced-graphene oxide (r-GO); patent landscape analysis; intellectual property landscape

1. Introduction

Graphene and its derivatives, such as graphene oxide (GO) and reduced graphene oxide (rGO), have shown significant potential in the field of dental implants due to their unique properties: mechanical strength, biocompatibility, antibacterial properties and osseointegration.

Graphene is a two-dimensional (2D) single layer of graphite, comprising sp^2-hybridized carbon atoms arranged in a hexagonal honeycomb lattice.

Graphene oxide is produced through the oxidation and exfoliation of graphite. GO is distinguished by the presence of carbonyl, hydroxyl and epoxide functional groups.

The most commonly utilized materials for dental implants are pure titanium (Ti) and its alloys. However, these materials lack the capacity to bind directly to bone or to stimulate new bone formation due to their inherent biologic inertness, thereby increasing the risk of implant failure. Recent studies have provided evidence that modifying the surface properties of the implant with carbon allotropes (in particular, graphene family nanomaterials, including graphene oxide (GO) and reduced GO (rGO)), could be an effective solution to this problem [1].

The incorporation of graphene and its derivatives into dental implants has been demonstrated to enhance biocompatibility by facilitating osseointegration through augmented cell adhesion and proliferation. This ensures the implant's stability and longevity.

Furthermore, scientific evidence substantiates the anti-inflammatory, antibacterial and osteogenic properties of these compounds.

The development of dental implants comprising graphene in the coated form of thin film represents a novel and promising avenue of research with the potential to enhance the efficacy of these treatments and reduce the incidence of complications such as infection and implant failure [2].

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While several bibliometric studies have been published on the use of graphene-based materials, they have focused exclusively on scientific articles [3,4], rather than patents.

A review of the literature reveals a paucity of articles that report on a patent study of dental implants [5–7] that do not focus on carbon allotropes.

Patents are an essential source of technical knowledge [8] (p. 39) that may not be found anywhere else. In a recent paper [9] (p. 23), the author estimated that the number of substances (RN—Registry Number) found only in patents and not in other information sources (NPL—Non-Patent Literature) is 56.6%.

Even if the quantity of information is difficult to quantify, the rising number of patent applications demonstrates the growing importance of patents as a source of information. For instance, in 2022, the EPO (European Patent Office) received a total of almost 200,000 applications. In the year 2021, a total of 1.586 million patent applications were filed in China.

The objective of this study is to provide a patent landscape analysis of graphene and its derivatives in relation to dental implants.

2. Materials and Methods

A patent landscape is a specific type of patent search conducted with the objective of identifying the most recent inventions or studying the development of a particular technology.

The analysis is employed to inform strategic decision-making in the following areas:

- The identification of potential investment opportunities;
- The determination of research and development (R&D) priorities;
- The assessment of competitor activities;
- The assessment of the freedom to operate in introducing new products to the market.

The documents that have been subjected to search are those pertaining to granted patents, patent applications and utility models.

Espacenet [10] has been selected as the most appropriate database for the purposes of this research. The comprehensive coverage and free availability of the database are key factors in this decision. The bibliographic coverage is extensive, encompassing over 150 million documents, while the full text comprises more than 127 million documents.

The objective of a patent search is to identify documents that claim similar technical features, rather than merely matching words.

A patent search can be carried out in the following two ways:

- By keywords (an intuitive but subjective approach);
- By classification codes or citations (language-independent tools).

A more comprehensive search can be conducted by combining keywords (with Boolean and/or proximity operators) and classification symbols.

The most frequently utilized patent classification systems are the International Patent Classification (IPC) and the Cooperative Patent Classification (CPC).

The IPC is a hierarchical classification system. The highest level comprises 8 sections (A–H), which are further divided into 80,000 subdivisions.

The CPC represents an enhanced version of the IPC, featuring a greater number of subdivisions (250,000).

In order to retrieve relevant patents, two concepts were combined: dental implants and graphene compounds.

The aforementioned concepts were then translated into keywords and classification codes (listed in Table 1).

Classification symbols were retrieved using the classification search tool provided by the EPO [11] (typing specific and precise keywords) or the IPCCAT (IPC Categorization) tool provided by WIPO (World Intellectual Property Organization) [12] (adding an abstract of the invention). The IPCCAT system enables the automated categorization of textual data within the IPC framework. It facilitates the generation of IPC predictions for a given text at the Class, Sub-class or Main Group levels [13].

Table 1. List of retrieved classification codes (IPC and CPC).

Classification Code	Classification System	Definition
A61C8/00	IPC/CPC	Means to be fixed to the jawbone for consolidating natural teeth or for fixing dental prostheses thereon; dental implants; implanting tools
A61C13/00	IPC/CPC	Dental prostheses
C01B32/15	IPC/CPC	Nano-sized carbon materials
C01B32/182	IPC/CPC	Graphene
C01B2204/00	CPC	Structure or properties of graphene
C01B32/198	IPC/CPC	Graphene oxide (GO)
C08K3/042	CPC	Uses of inorganic substances as compounding ingredients—graphene or derivatives
B82Y *	IPC/CPC	Specific uses or application of nanostructures
C04B35/46	IPC/CPC	Ceramic products based on titanium oxides
C04B35/48		Ceramic products based on zirconium or hafnium
A61L37 *	IPC/CPC	Materials for prosthesis or for coating prosthesis

* and subsequent subgroups.

In order to identify all relevant applications, a search was carried out on the Espacenet database using the following parameters: title abstract claims (TAC) and the full-text fields, in addition to both classification systems (IPC and CPC).

The initial query, comprising solely keywords, yielded 42 results. In contrast, the final query, which combined keywords with classification symbols, produced 71 results.

The final query is as follows:

((cl all "C04B35" OR cl all "A61L27") AND (ctxt all "graphene" OR ctxt=("graphene " prox/ordered "oxide") OR ctxt=("reduced graphene" prox/ordered "oxide") OR ctxt all "r-GO") AND (ftxt=("dental " prox/distance<3 "implants") OR cl any "A61C")) OR ((ctxt all "dental implant?" AND (ctxt all "graphene" OR ctxt=("graphene " prox/ordered "oxide") OR ctxt=("reduced graphene" prox/ordered "oxide") OR ctxt all "r-GO")) OR (ctxt all "dental implant?" AND (cl =/low "C01B32/182" OR cpc =/low "C01B2204/00" OR ((cl =/low "C01B32/15" OR cl =/low "B82Y") AND ctxt all "graphene" AND ctxt=("graphene" prox/ordered "oxide")) OR cpc =/low "C08K3/042")) OR (cl all "A61C" AND (cl =/low "C01B32/182" OR cpc =/low "C01B2204/00" OR ((cl =/low "C01B32/15" OR cl =/low "B82Y") AND ftxt all "graphene" AND ftxt=("graphene" prox/ordered "oxide") AND ftxt=("reduced graphene" prox/ordered "oxide") AND ftxt all "r-GO") OR cpc =/low "C08K3/042"))).

3. Results and Discussion

Following the initial screening of the title, abstract and claims, 16 documents were excluded from the analysis as they were deemed to be off-topic and not related to the use of graphene or its derivatives in dental implants.

The first patent application was filed in 2010.

The patenting trend shows an increase in filing numbers starting from 2014 onwards (as shown in Figure 1).

The data retrieved from Espacenet were transferred to the Orbit Patent Intelligence platform [14], which was used to analyze the data.

The graph in Figure 2 illustrates the top priority countries.

China has the highest number of applications with 20, followed by the USA with 7 and South Korea with 6. A significant number of applicants have used the PCT system, which is not a granting system but rather a procedure to postpone entry into the national or regional phases.

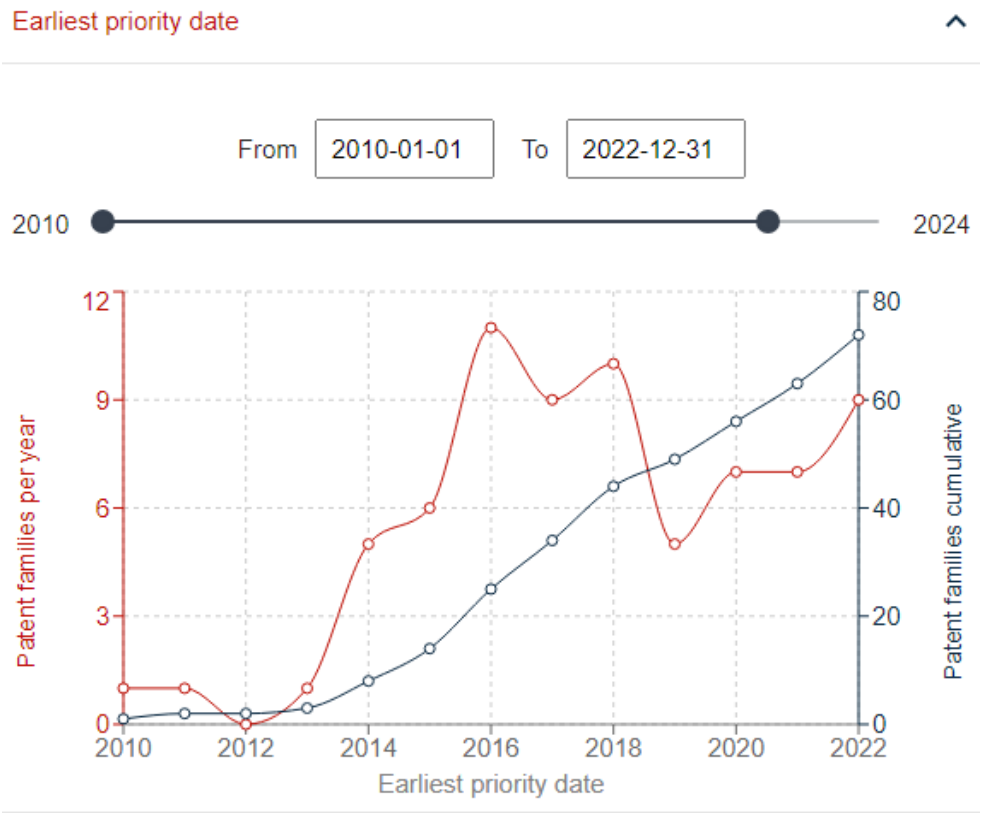

Figure 1. Patenting trend from 2010 to 2022 (source: Espacenet).

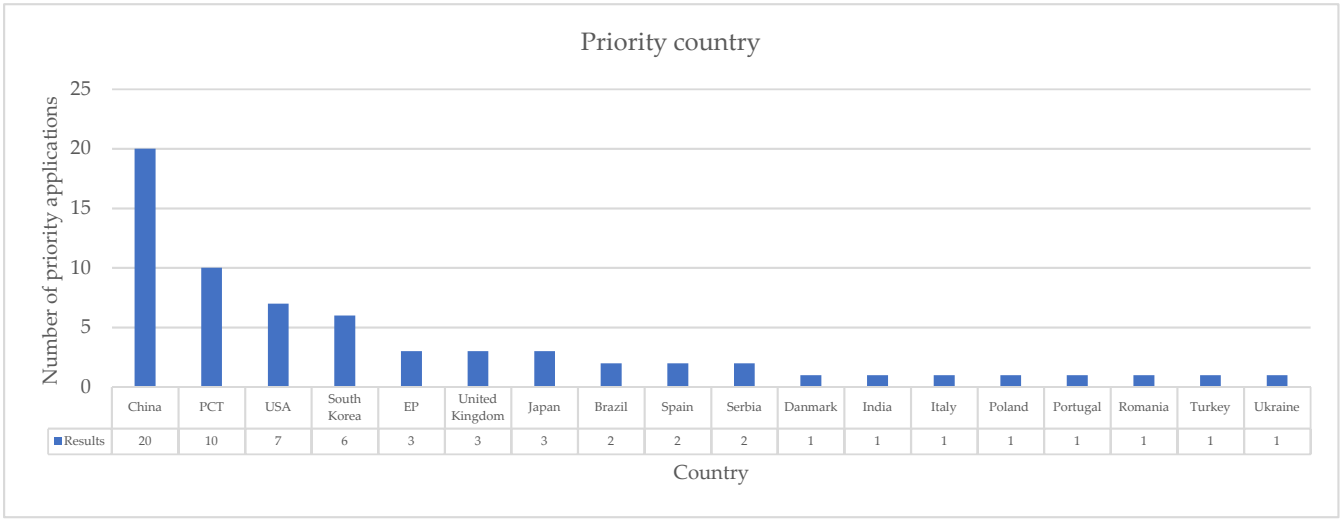

Figure 2. Number of patent applications filed in priority countries (source: Orbit).

A total of 55.8% of applications were granted, 26.9% are currently under examination, 11.5% have lapsed due to the failure to pay the annual fees, and 5.8% have been revoked by the Patent Office for failing to meet the patentability requirements or have been withdrawn by the applicant (see Figure 3).

The majority of applications were found to involve GO, with graphene and r-GO also being employed to a lesser extent (Figure 4a).

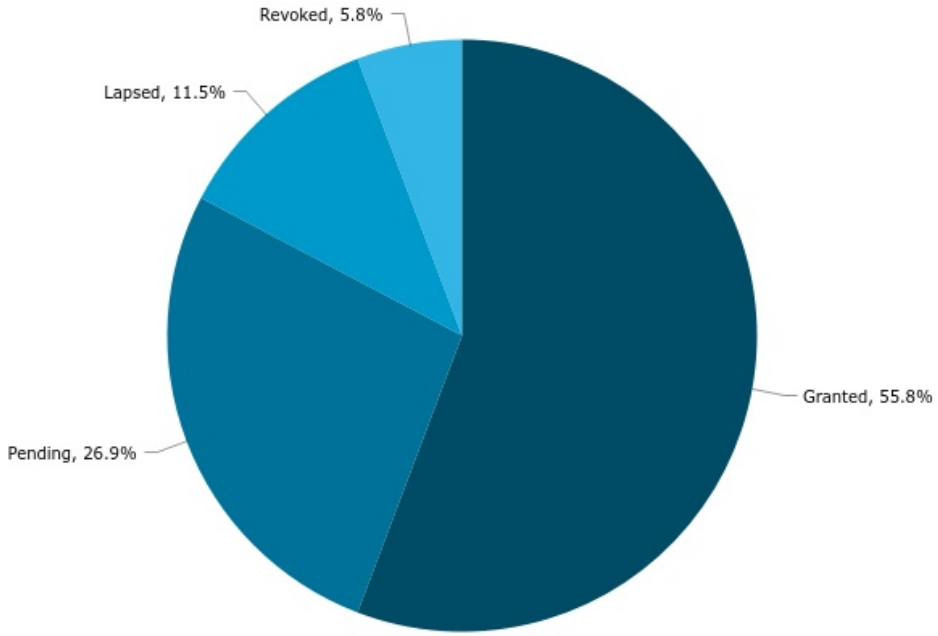

Figure 3. Legal status of retrieved documents (source: Orbit).

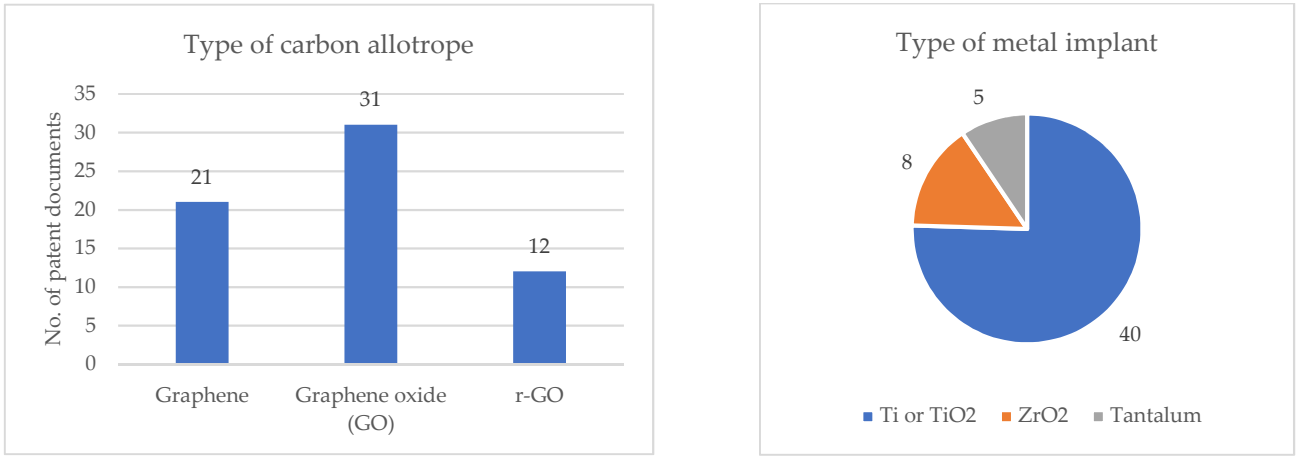

Figure 4. (**a**) Type of claimed carbon allotropes; (**b**) type of claimed metal implants.

Titanium and its alloys are among the most frequently used materials.

A limited number of applications have been identified that claim the presence of zirconium and tantalum (Figure 4b).

These findings are consistent with those reported in the scientific literature [15,16]. Titanium or titanium alloy continues to be the material of choice in the fabrication of dental implants [17].

The selection of graphene or graphene oxide for use in dental implants is dependent upon the specific requirements and desired properties of the intended application.

The exceptional mechanical strength of graphene has the potential to significantly enhance the durability and structural integrity of dental implants [2]. While pure graphene is biocompatible [18], its hydrophobic nature may restrict its interaction with biological fluids and cells. Furthermore, it exhibits reduced chemical reactivity in comparison to graphene oxide [19].

GO contains a variety of reactive oxygen functional groups, including hydroxyl, carboxyl and epoxy groups, which impart high hydrophilicity and numerous potential

sites for functionalization. This enables the attachment of biomolecules, drugs and other therapeutic agents. The properties of graphene oxide (GO) can be influenced by several factors, including the starting materials used, the synthesis method employed and the degree of oxidation [20]. The functional groups present in GO have been demonstrated to enhance cell adhesion, proliferation and differentiation, thereby promoting improved integration with the bone.

The findings of an in vitro investigation indicated that GO-coated titanium dental implants possess augmented osteogenic potential and antimicrobial efficacy [21].

4. Conclusions

The objective of this study was to present a comprehensive methodology for the retrieval of patent documents. A patent landscape analysis may prove beneficial in the context of a subsequent technology transfer project. In this case, a researcher could commence the modification of a titanium implant with graphene oxide (GO), a linker and an additional component (which should be novel and inventive to be patentable).

Global patenting is led by China and the USA. The patenting trend shows an increase in filing numbers starting from 2014 onwards.

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