Systematic Patent Review of Nanoparticles in Drug Delivery and Cancer Therapy in the Last Decade

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Abstract: Background: The application of nanotechnology has been considered a powerful platform in improving the current situation in drug delivery and cancer therapy, especially in targeting the desired site of action.

Objective: The main objective of the patent review is to survey and review patents from the past ten years that are related to the two particular areas of nanomedicines.

Methods: The patents related to the nanoparticle-based inventions utilized in drug delivery and cancer treatment from 2010 onwards were browsed in databases like USPTO, WIPO, Google Patents, and Free Patents Online. After conducting numerous screening processes, a total of 40 patents were included in the patent analysis. See the PRISMA checklist 2020 checklist.

Results: Amongst the selected patents, an overview of various types of nanoparticles is presented in this paper, including polymeric, metallic, silica, lipid-based nanoparticles, quantum dots, carbon nanotubes, and albumin-based nanomedicines.

Conclusion: Nanomedicines’ advantages include improvements in terms of drug delivery, bioavailability, solubility, penetration, and stability of drugs. It is concluded that the utilization of nanoparticles in medicines is essential in the pursuit of better clinical practice.

Keywords: Nanoparticles, drug delivery, cancer, polymeric, magnetite, quantum dots, patents, bioavailability.

1. INTRODUCTION

According to the National Nanotechnology Initiative, NNI, nanotechnology is the science and understanding of materials or matters where the diameters range from 1 to 100 nm, generally [1]. This definition continues to be used by numerous federal offices, which include the United States Food and Drug Administration (FDA), as well as the Patent and Trademark Office (PTO) [2]. However, this particular definition restricted to the size limitation may not be accurate since nanomaterials having sized up to a few hundred nanometers can still have their unique properties. Accordingly, the National Institute of Health introduced an alternative definition that does not depend on sizes, since nanotechnology has a wider range of uses and is being used in various fields [2].

In 1959, Richard Feynman initiated the thought process of nanotechnology by introducing the idea of manipulating matter at an atomic level when he presented the lecture with a title of ‘There’s Plenty of Room at the Bottom’ during the American Physical Society Meeting [3]. The concept and hypotheses developed by Feynman were then confirmed, and proven to be correct. Thereupon, he was awarded the Nobel Prize in Physics 1965. After almost 15 years from Feynman’s lecture, in 1974, the term ‘nanotechnology’ was used for the first time by a Japanese scientist, Norio Taniguchi [4]. It was in the 1980s that the nanotechnology golden era began, when the first nanoparticle, ‘Fullerene’ or ‘Buckyball’, was discovered by three researchers named Smalley, Kroto, and Curl [3].

Another justification of the said golden era was the release of the first book on nanotechnology titled ‘Engines of Creation: The Coming Era of Nanotechnology’ [5]. It was successfully published in 1986 by Eric Drexler from the Massachusetts Institute of Technology (MIT); Drexler used ideas from Feynman’s lecture and Taniguchi’s terminology of nanotechnology. The advancement of the nanotechnology field was further expanded when another scientist from Japan, Sumio Iijima, invented carbon nanotubes in 1991 [6]. In addition, researches on nanotechnology were considered a national priority for the United States after President George Bush signed the 21st Century Nanotechnology Research and Development Act in 2003 [3]. Due to the referred enactment, the funding of the National Nanotechnology Initiative...
(NNI), a research and development (R&D) program, was increased.

The overlapping approach of nanotechnology with medicines has led to the formation of an interdisciplinary field of nanomedicine. Though it is considered relatively new, the field is rapidly developing and has revolutionized the 20th century [7]. Nanomedicine is primarily the major application of nanotechnology; according to the National Science Foundation (NSF), 1/3 of patents in the nanotechnology field will comprise of biomedical applications by the year 2020 [2]. Furthermore, nanomedicine is a field that studies biology by the utilization of nanotechnology instruments and concepts, and involves developing biological molecules to have capacities that vary from those that they initially have. Some of the areas in which nanoparticles are implemented in medicines include drug delivery, medical diagnosis, burn and wound treatments, antimicrobials, dentistry, gene therapy, and therapeutics, such as applications in various diseases like cancer and Alzheimer’s disease.

It is essential for drugs to be delivered to the desired site in a controlled manner while keeping the medications’ adverse effects at a minimum level. Therefore, targeted drug delivery allegedly has been considered to be one of the primary uses in nanomedicine. Due to the nanoparticles’ small size, thus, large surface area, both the bioavailability of the drugs and the accuracy of the biodistribution may be increased [8]. Besides therapeutic uses, nanoparticles can also be applied in diagnostic imaging due to their ability to enhance and upgrade the contrast of spectroscopy. Taking a specific example of superparamagnetic iron oxide nanoparticle (SPION), which helps with the early detection of liver metastases as it has been shown to improve the results from Magnetic Resonance Imaging (MRI) [9]. Also, due to their antimicrobial properties, paints containing silver nanoparticles are now being used, especially in indoor medical settings like hospitals [10]. As can be seen, nanotechnology offers a wide range of applications in the medical field, and there is hardly any area of medicine that would not gain the positive effects that nanotechnology provides [11].

One of the many benefits of using and applying nanotechnology in medicine, for example in targeted drug delivery, is improved efficacy. This may be due to the enhancement of drug solubility, hence, obtaining increased bioavailability [12]. In some cases, nanomedicines, depending on the type of nanoparticles used, may have a lower toxicity profile compared to when conventional drugs are administered [13]. Another positive aspect of nanomedicine is that the pharmacokinetic and/or pharmacodynamic properties can be altered to be more desirable [12]. Some of the pharmacokinetic advantages include specific delivery of the drug, increased metabolic stability, better membrane permeability, and prolonged drug action [14]. Whereas, an increased maximum concentration (Cmax) and a shorter time to achieve maximum concentration (Tmax) are some of the pharmacodynamic advantages that nanomedicines may carry [14]. However, there are many different types of nanoparticles applied in the field of medicine, and each type will have its specific approach as to how they will aid the nanomedicine’s benefits.

Some of these nanomaterials will be further elaborated in this paper.

Despite the numerous advantages that nanomedicines possess, some challenges need to be addressed and taken into account. This includes biological challenges; one of the primary reasons why nanomedicines fail in clinical trials is due to less research committed to understanding the relationships between the behavior of nanomedicines and patients’ biology in specific clinical cases and disease heterogeneity [15]. Overcoming the biological barriers is vital to ensure that the targeting of the diseased tissue is improved, and the accumulation of drugs in organs that are not targeted is reduced. Another factor that can limit nanomedicines’ availability in the market is biocompatibility, as whether or not the materials are compatible with the living tissue. Hence, to ensure that the particular medication is safe to be used in humans, detailed toxicology is essentially required [16].

When a novel technology is being invented, those responsible for the inventions can patent the product or process. Patent, which is intellectual property, is important to protect inventions and innovations from being used by other inventors and industries illegitimately or for commercial purposes. Patents can be used to explore the current existing art of a particular field. For example, in the pharmaceutical industry, patents from various databases can be surveyed to recognize the development of its technological changes [17].

The main objective of this literature review is to survey and review patents related to the two particular areas of nanomedicines, which are drug delivery and cancer therapy, from the past ten years. Another objective is to summarize the said patent technologies, and where possible, some related research within each application area will also be included, to an extent. The elaboration of the methodology for this patent review is summarized in Table 1 below. The steps included are the formulation of the study hypothesis, location of study, collection of data, critical evaluation of studies, analysis and presentation of data, and lastly, data interpretation.

The patents' browsing was conducted from September to November 2021 through the search from databases like USPTO (United States Patent and Trademark Office), WIPO (World Intellectual Property Organization), Google Patents, and Free Patents Online. The keywords used are tabulated in Table 2 below; but the major search terms used were “nanoparticles,” “nano*,” “drug delivery,” and “cancer.” The searched patents were selected if the following inclusion criteria were met:

- Full-text patents that were written in English.
- Patents’ publication year of 2010 (inclusion) up until 2020.
- Patents related to nanoparticles used in medicine, in particular, drug delivery and cancer therapeutics only.

On the other hand, patents involving nanoparticles with non-medical uses or those with limited application for a diagnostic purpose only, or duplicate patents were excluded from the review analysis.
There are two main points highlighted in this review concerning nanoparticles used in medicine: drug delivery and cancer therapeutics. The patent search for the respective points was done separately using the keywords mentioned above. In order to obtain relevant patents in accordance with the eligibility criteria, the titles and abstracts of the patents searched from the databases were initially screened. Following that, the full texts of all the relevant patents were examined and analyzed to ensure that they are meeting the defined eligibility criteria.

A flowchart diagram showing the different phases of the search process in the patents’ selection is presented in Fig. (1). For drug delivery-related patents: 109 out of 982 possibly relevant patents retrieved from USPTO, WIPO, Google Patents, and Free Patents Online databases were excluded from the analysis due to duplication. The titles and abstracts of the remaining 873 patents were then screened for eligibility criteria, and a total of 828 irrelevant patents were further excluded. Finally, after the full-text screening, only 20 out of 45 related patents were included to be analyzed and discussed in this review. Whereas, for cancer therapeutics-related patents, 455 relevant patents were initially retrieved from the mentioned databases. There were 112 duplicates; therefore, only 344 records were preserved for title and abstract screening. Following the screening, 306 publications were then excluded from the analysis. After assessing the texts thoroughly, 20 out of 38 patents were eventually selected for detailed discussion in the literature review.

2. NANOPARTICLES FOR DRUG DELIVERY

In this section, nanoparticles-mediated drug delivery will be further explained in details with the aid of patents listed in Table 3 as well as relevant scientific articles to support the respective inventions. The patents listed are classified based on the system that is targeted by the nanomedicine such as ophthalmic, transdermal, topical, and oral drug delivery systems.

2.1. Polymeric Nanoparticles

The US Patent 9,149,440 B2 invented by Turos and Shim relates to preparing nanoparticles bearing chemically modified bioaffecting agents using microemulsion polymerization. The invention describes the novel technique of preparation of the polymeric nanoparticles with the ‘targeted materials’ bonded to the particles' surface using microemulsion polymerization [18]. The process results in the polymeric nanoparticles to be homogenously distributed in an aqueous state without the presence of toxic material. The ‘targeted materials’ mentioned implicates the bio-affecting agents...
**Fig. (1).** Flowchart of patents selection.

**Table 3. Relevant patents on drug delivery mediated by nanoparticles.**

| Sr. No. | Patent No. | Classification | Patent/Publication Title | Inventor(s) | Organization | Issue/Publication Date | References |
|--------|------------|----------------|--------------------------|-------------|--------------|------------------------|------------|
| 1      | US 8,859,004 B2 | Based on type of NP: Polymeric | pH-Sensitive Nanoparticles for Oral Insulin Delivery | Zhang L, Ling L, Zhou LY, Wu ZM, Guo XD, Jiang W, Luo Q, Qian Y | Nano and Advanced Materials Institute Limited, The Hong Kong University of Science and Technology, HK | Oct. 14, 2014 | [22] |
| 2      | US 9,149,440 B2 | Based on type of NP: Polymeric | Nanoparticles for Drug-Delivery | Turos E, Shim Jy | University of South Florida, US | Oct. 6, 2015 | [18] |
| 3      | US 10,555,911 B2 | Based on type of NP: Polymeric | Highly Penetrative Nanocarriers for Treatment of CNS Disease | Zhou J, Patel TR, Piepmeier JM, Saltzman WM | Yale University, US | Feb. 11, 2020 | [23] |
| 4      | US 9,370,488 B2 | Based on type of NP: Lipid | Method and System for Synthesizing Nanocarrier Based Long Acting Drug Delivery System for Insulin | Hamidi M | Kimia Zist Parsian (KZ); Tehran, IR | Jun. 21, 2016 | [24] |

(Table 3 contd....)
| Sr. No. | Patent No. | Classification | Patent/Publication Title | Inventor(s) | Organization | Issue/Publication Date | References |
|---------|------------|----------------|--------------------------|-------------|--------------|------------------------|------------|
| 5       | WO 2018/031782 A1 | Based on type of NP: Lipid | Nanoparticle Compositions and Methods for Enhanced Stability and Delivery of Glycopeptide Drugs | Polt R, Heien ML, Pemberton JE | The Arizona Board of Regents on behalf of The University of Arizona | Feb. 15, 2018 | [26] |
| 6       | WO 2013/176468 A1 | Based on NP type: Metallic (Gold) | Liver Targeted Drug Delivery Systems Using Metal Nanoparticles and Preparing Method Thereof | Hahn SK, Lee MY, Yang J, Jung HS | Postech Academy Industry Foundation, KR | Nov. 28, 2013 | [34] |
| 7       | WO 2014/047318 A1 | Based on type of NP: Metallic (Iron Oxide) | Delivery of Therapeutic Compounds with Iron Oxide Nanoparticles | Kaittanis C, Grimm J | Memorial Sloan-Kettering Cancer Center, US | Mar. 27, 2014 | [30] |
| 8       | US 10,456,363 B2 | Based on type of NP: Metallic (Iron Oxide) | Modified Cyclodextrin Coated Magnetic Nanoparticles for Targeted Delivery of Hydrophobic Drugs | Joy P, Naduvilidam JK | Council of Scientific & Industrial Research, IN | Oct. 29, 2019 | [31] |
| 9       | WO 2018/102921 A1 | Based on type of NP: Metallic (Gold) | Ultrastable Gold Nanoparticles for Drug Delivery Applications and Synthesis Thereof | Boisselier E, Ouellette M, Pernet V, Omar M | Universite Laval, CA | Jun. 14, 2018 | [33] |
| 10      | US 8,535,726 B2 | Based on type of NP: Carbon | Supramolecular Functionalization of Graphitic Nanoparticles for Drug Delivery | Dai H, Liu Z, Li X, Sun X | The Board of Trustees of the Leland Stanford Junior University, US | Sep. 17, 2013 | [39] |
| 11      | WO 2014/015334 A1 | Based on NP type: Carbon | System and Methods for Nanosstructure Protected Delivery of Treatment Agent and Selective Release Thereof | Wu CH, Kim JH, Xu J | Brown University, US | Jan. 23, 2014 | [40] |
| 12      | WO 2019/113184 A1 | Based on type of NP: Silica | Nanoparticles for Nerve Penetration and Uses Thereof | Kohane DS, Liu Q | Children's Medical Center Corporation, US | Jun. 13, 2019 | [43] |
| 13      | US 10,729,783 B2 | Based on type of NP: Silica | Hollow Silica Nanoparticles with Encapsulated Bioactive Ingredients, Preparation Process and Applications Thereof | Mou CY, Kou NY, Wu SH, Chen YP | National Taiwan University, TW | Aug. 4, 2020 | [41] |
| 14      | WO 2018/167618 A1 | Based on type of NP: Quantum Dot | Light Responsive Quantum Dot Drug Delivery System | Naasani I | Nanoco Technologies Ltd., GB | Sept. 20, 2018 | [46] |
| 15      | US 8,273,366 B2 | System-based: Ophthalmic | Ophthalmic Drug Delivery System | Chauhan A, Gulsen D | University of Florida Research Foundation, Incorporated, US | Sep. 25, 2012 | [47] |
| 16      | US 10,729,663 B1 | System-based: Ophthalmic | Nanoparticles in Thermoreversible Gels for Enhanced Therapeutics | Sutariya VB, Hirani AA, Pathak YV | University of South Florida, US | Aug. 4, 2020 | [48] |
| 17      | US 8,467,868 B1 | System-based: Transdermal Based on type of NP: Hyaluronic acid | Method of Transdermal Drug Delivery | Mohapatra SS, Kumar A, Bishwabhusan S | University of South Florida, US | Jun. 18, 2013 | [49] |
| 18      | US 9,233,110 B2 | System-based: Topical/skin | Protein Nanocarriers for Topical Delivery | Perumal OP, Averineni RK, Podarilla SK, Alqahtani M | South Dakota State University, US | Jan. 12, 2016 | [50] |
| 19      | WO 2014/197640 A1 | System-based: Oral | Novel Core-Shell Nanoparticles for Oral Drug Delivery | Perumal O, Alqahtani SA | South Dakota State University, US | Dec. 11, 2014 | [51] |
| 20      | WO 2020/086871 A1 | System-based: Oral | Functionalized Nanoparticle Formulations for Oral Drug Delivery | Anchordooqy T, Graner M, Betker J, Angle B | The Regents of The University of Colorado, A Body Corporate, US | Apr. 30, 2020 | [52] |
or the targeted drug, and these include a broad range of drug classes including analgesics, anti-inflammatory agents, antibiotics, antivirals, anticoagulants, antihypertensives, and many more. Chemical modification of the targeted bio-afflicting agents is performed so that incorporating the drug on to the surface of the nanoparticle is possible; the size of the polymeric nanoparticles can range from 1 to 1000 nm, but the most preferred size is between 1 and 200 nm. The aim of the drug bearing nanoparticles with target molecules bonded to the surface is to protect them from disruption by outer intervention either in vivo or in vitro, ensuring environmental stability and selectivity. The intervention also allows the drug delivery of highly viscous agents or drugs insoluble in water to be improved.

Diabetes, a condition where the glucose level in the blood is high, is considered one of the leading causes of mortality globally, and results in a lower life expectancy [19]. According to the International Diabetes Federation (IDF), the prevalence of diabetes is estimated to be 693 million by 2045 on a worldwide basis, thus, raising the concerns to reduce the rate of death as a consequence of diabetes [20]. Daily administrations of insulin are crucial for the survival of diabetic patients, especially those with Type 1 diabetes, which aim to increase the patients’ quality of life in general. However, currently, the most commonly used route of insulin administration is by subcutaneous injections [21]. This particular administration route can reduce the patients’ compliance due to the fear of injecting their own skin.

Although oral administration is the most broadly acknowledged type of route to deliver drugs, it is not possible to deliver peptide and protein drugs, like insulin, to the targeted site directly as the digestive juices in the stomach can break it down. Therefore, it is worth to note that Zhang et al. have disclosed their invention (US8859004B2), which is composed of insulin-loaded polymeric pH sensitive nanoparticles. The pH-sensitive nanoparticles are useful for biopharmaceutical technology industry. The particular polymer used to prepare the design is HP55, which is typically used in pharmaceutics to manufacture enteric-coated polymers. In addition, multiple emulsions solvent evaporation is used to process the pH-sensitive nanoparticles for oral insulin delivery (Fig. 2). The invention advantageously allows the nanomedicine to stabilize in the stomach’s acidic environment and thus releases the insulin in the intestinal environment in a controlled manner. Not only that, but an improvement with 10% bioavailability after oral administration was also observed. A significant reduction in blood glucose with the insulin-loaded nanoparticles was observed in diabetic rats induced by Streptozotocin [22].

Last but not least, among the numerous obstacles in delivering drugs to the desired targeted site, the blood brain barrier (BBB) is one of the main challenges to conquer, especially for drug delivery in the central nervous system. The patent US10555911B2 describes an invention of polymeric nanoparticles that can penetrate the brain, where drugs can be loaded into the nanoparticles in particular for treatment of glioblastoma [23]. The procedure that can be used to manufacture the nanoparticles is the single-emulsion method. As mentioned in the patent, polymers, such as poly(lactic acid) (PLA), poly(lactic-co-glycolic acid) (PLGA), and others, can behave as the nanocarriers. The diameters of these nanocarriers are less than 100 nanometers, preferably 25 to 75 nm, in order to be able to penetrate the blood brain barrier. Due to its penetration ability, this invention is incredibly valuable for the treatment of brain tumors as it can pass through the brain’s area that encompasses the tumors.

### 2.2. Lipid Nanoparticles

As opposed to the polymeric nanoparticles for oral administration of insulin described above, the patent US9370488B2 by Mehrdad Hamidi is associated with the synthesis of lipid-based nanoparticle for injective administration of insulin [24]. The invention is related to nanomedicines or nanocarrier based drug delivery systems and allows the insulin to be entrapped by the nanocarrier, made up of lipids, phospholipids, organic solvent, and polymers. The procedure to develop the nanocarrier is explained in the patent; in brief, lipids and phospholipids are dissolved in an organic solvent, for example, ethanol or methanol, and this mixture acts as the core, which is then coated or enveloped by polymers such as polyvinyl alcohol and polyethylene glycol. Also, the entrapment of insulin to the nanocarrier is feasible due to the effect of anti-solvency. A powdered form of the mixture can also be made to ensure better storage of the nanomedicine. The invention aims to develop a long-acting delivery system for insulin, releasing the hormone in a slow and controlled manner. Therefore, allowing the prolonged release of insulin reduces the frequency of injective administration, and possibly increases the patient's adherence to the medications [25]. The illustration depicts both the insulin systems (Fig. 2).

Next, another patent publication that relates to the lipid-based nanoparticles is the WO2018031782A1 for enhancing stability and delivery of glycopeptide drugs [26]. It provides information about the drug delivery system of solid lipid nanoparticles (SLN) that can administer glycopeptide drugs in vivo. The glycopeptides are integrated into the SLN, concurrently enabling the nanomedicine to mimic how lipoproteins carry materials in the blood. Moreover, the lipid nanoparticles prevent the drugs' peptide chains from being broken down by enzyme peptidases long enough until the glycopeptides reach the targeted site. All in all, the whole system aims to deliver the glycopeptide drugs better and to improve the drugs' stability. In comparison to polymeric-based nanoparticles, biocompatible or biodegradable materials are used in the preparation of solid lipid nanoparticles (SLN), thereby resulting in better tolerability and lower cytotoxicity. Additionally, the drug loading, a process of integrating drugs into matrix or micelles, of SLN is of higher capacity than polymeric nanoparticles, and producing solid lipid nanoparticles is also considered economically efficient [27].
2.3. Metallic Nanoparticles

At present times, different types of metallic nanoparticles have been studied, researched, and considered in the application of targeted or sustained drug delivery systems. The unique physical and chemical properties allow the materials to be taken into consideration. These properties include and are not limited to the large surface area, electrostatic charge, and potential positive response to photothermal therapy. Therefore, the materials enable a high dosage of drugs to be incorporated in the nanomedicine, and the drug permeability may also be increased when the first-pass metabolism is overcome [28]. Moreover, the metallic nanoparticles can be modified by binding the materials with specific functional groups that can further expand the applications of metallic NPs in medicine [29]. Some of the typical metallic nanoparticles are gold, silver, iron oxide, gadolinium, and platinum. In this review, the recent patents of the decade that relate to metal-based nanoparticles applied in the field of drug delivery are included.

Firstly, the patent publication WO2014047318A1 reflects methods to deliver therapeutic agents using metallic iron oxide nanoparticles, IONPs, to the desired target site [30]. The system comprises of iron oxide nanoparticle core that has superparamagnetic properties. This invention conveniently allows the entrapment of unmodified drugs onto the external surface of the nanoparticles. Usually, therapeutic agents loaded onto nanodrug delivery systems, apart from metallic nanoparticles, like polymeric, lipid, and albumin-based, the drugs are generally altered. The alteration may be due to the binding or conjugation of the medications with other molecules. Therefore, when this happens, the modified drug is deemed a ‘new’ drug; hence, it needs to undergo clinical trials again. Advantageously, in contrast, the therapeutic agent for this invention is only attached, non-covalently, to the coating of the iron oxide nanoparticle, maintaining the drugs' original structure and function. The system can be useful in targeted combinatorial therapy for cancer, where the administered loaded agents' stability and bioavailability can be improved significantly.
Similarly, the patent US10456363B2 involves the utilization of magnetic iron oxide nanoparticles, IONPs, as well [31]. In brief, the invention aims to aid in targeted drug delivery of hydrophobic drugs by developing suitable nanocarrier for these agents. The drugs are loaded into a nanocarrier made up of magnetite nanoparticles, and the said nanocarrier is coated by β-cyclodextrin-citrate. According to Lakkakula and Krause (2014), cyclodextrins are especially useful in improving the solubility of drugs that are hydrophobic [32]. Alternatively, gold nanoparticles (AuNPs) are mainly used in the invention of WO2018102921A1, where the nanoparticles are considered ultra-stable as the AuNPs can endure both cold treatments, like freeze-drying, and heat-like treatments, and remain unchanged at the end of the procedures [33]. The particular invention is utilized in delivering therapeutic agents to mucous membranes; thus, it can be used to treat diseases or disorders associated with drug administration to the mucosal membranes, such as for glaucoma and conjunctivitis. The gold nanoparticles can interact with the mucous membrane, allowing a prolonged exposure of the drug to the desired site, possibly resulting in the reduction of the medications' dosing frequency. In addition, the administration of the nanomedicines can be through oral, topical, or even via aerosol.

Another nanodrug delivery system comprising of gold nanoparticles is described in the patent publication WO2013176468A1 for liver targeted drug delivery system. The patent publication provides information on the methods to prepare modified gold nanoparticles for targeted hepatic drug delivery using AuNPs [34]. Hyaluronic acid (HA) is implemented as carriers in the structure of the invention, as it is characterized in having particular delivery property to liver tissues. This is because of the presence of large quantities of HA receptors in specific tissues, including the liver, kidney, and even tumor cell surface [35]. Since gold nanoparticles are compatible with the living tissues, and hyaluronic acid, too, have biocompatible, biodegradable, and liver specific targeting property, therefore, the system can be used in delivering therapeutic drugs to the liver more safely and effectively for the treatment of liver-related diseases, such as hepatitis.

2.4. Carbon Nanoparticles

As indicated in section 2.2, under the History of Nanotechnology, carbon nanotubes (CNTs) were initially discovered by S. Iijima in 1991 [3]. Carbon nanotubes, as the name suggests, are made up of carbon and have a tubelike structure that appears as a cylinder. The arrangement of the CNTs can be designated as single-wall or multiwall, with or without open ends. Single-wall nanotubes (SWNTs) and multiwall nanotubes (MWNs) are composed of one or more layers of graphene, respectively [36, 37]. Carbon nanotubes are considered excellent candidates of nanodrug carriers in delivering therapeutic agents because of their capability to directly penetrate cells through the cytoplasmic and nuclear membrane [37, 38]. However, CNTs toxicity is one of the significant issues concerning carbon nanotubes; various approaches and strategies are being studied to overcome this problem.

A patent, US8535726B2, titled Supramolecular Functionalization of Graphitic Nanoparticles for Drug Delivery, relates to the application of carbon nanotubes in the area of drug delivery [39]. The system encompasses a complex made up of carbon nanotube, particularly single-wall carbon nanotube (SWNTs), attached with hydrophilic polymers, thereby allowing the system to be stable in an aqueous suspension form. Targeting agents, such as antibodies or Arginylglycylaspartic acid (RGD) peptide, may also be associated with the complex so that targeted delivery of drugs into specific cell types can be better achieved. The nanomedicine advantageously offers the delivery of therapeutic agents into the inside of the targeted cells.

Another patent publication related to carbon-based nanoparticles, WO2014015334A1, relates to treatment agent and initiation of effective and temporally-regulated release of the agent at site. The invention describes carbon nanotubes’ involvement as drug delivery carriers in which therapeutic agents are encapsulated and isolated in a temperature-sensitive hydrogel [40]. Moreover, the nanostructure's external surface can be appropriately altered chemically depending on which relevant functions are intended to be addressed, for example, in terms of therapeutic agents’ absorption, drug solubility, sensitivity to pH, temperature, or other environments. The application of inductive heating raises the temperature of the complex, and as a result, triggers the drugs to be controllably released from the nanostructure into the desired body site. Due to the gel's surface tension and viscosity, the treatment agents remain enclosed in the nanotube when no inductive heating is applied.

2.5. Silica Nanoparticles

Silicon dioxide or silica-based nanoparticles show great potential in the implementation of drug carriers. This is because of the fact that the nanoparticles have unique mesoporous structures and large surface areas that give rise to high loading capacity for the therapeutic agents. Moreover, due to their chemical and thermal stability, good biocompatibility with living tissues, and low level of toxicity, these make silica nanoparticles well-qualified candidates in the application of targeted and controlled delivery of bioactive agents [41, 42]. A patent, US10729783B2, describes an invention that relates to silica nanoparticles, in particular hollow silica nanoparticles (HSNs) acting as a drug delivery system for loading bioactive ingredients [41]. The system comprises numerous layers of silica shells that have mesopores in each film. As indicated in the patent, the diameters of the mesopores should not exceed 5 nanometers. Additionally, just like most of the previous inventions from other types of nanoparticles, therapeutic drugs can be encapsulated in the nanoparticles’ hollow structure. Due to the different layers of silica shells, it provides separate spaces where the therapeutic agents can be accommodated; in each area, similar or other suitable different drugs can be selected to be encapsulated, and last but not least, the referred drug should have a size bigger than the shells’ mesopores.
The numerous distinct tissue barriers around the site of action for nerve blockers’ administration cause the medication to penetrate poorly into the nerves; thus, the full potential of the drugs’ effectiveness is not achieved. As a consequence, higher concentration of the drug is needed for better efficacy. It is, therefore, worth noting the following relevant patent. The patent publication, WO2019113184A1 titled Nanoparticles for Nerve Penetration and Uses Thereof, provides information about the clinical application of hollow silica nanoparticles (HSNs) in delivering therapeutic agents specifically to the nerves [43]. The therapeutic agents can be and are not limited to nerve blockers, nerve growth factors, anti-inflammatory medications, steroids, antibiotics, and antivirals; the selected drugs can be loaded into the hollow structure of silica nanoparticles. The patent also reflects the local route of administration of the nanomedicine at the patient’s sciatic nerve. In comparison to free nerve blockers, which means not encapsulated by the HSNs, the invented nanomedicine advantageously improves the penetration of the referred drug into the nerve, increases the rate to achieve the desired effect, and prolongs and extends the therapeutic effect of the nerve blocker.

2.6. Quantum Dot Nanoparticles

Quantum dots are nanocrystals of semiconductors. Some of the common materials incorporated as quantum dots for applications in medicines include cadmium such as cadmium selenide (CdSe) and cadmium telluride (CdTe), and indium such as indium arsenide (InAs) and indium phosphide (InP) [44]. Quantum dots, QDs, have unique optical properties, excellent photostability, which means that when they are exposed to light, they will not be rapidly and readily degraded. They also have adequate surface area for the attachment of therapeutic agents for quantum dot-based drug delivery systems (QD-DDS). Like most of the other NPs, this type of nanoparticles can also undergo alteration or modification by linking suitable molecules to the surface for the betterment of drug delivery. Liquid crystals are suitable to release sufficient drug load to be effective against cervical cancer cell line [45].

Naasani (2018) patented (WO2018167618A1) an invention associated with QD-DDS with a title of Light Responsive Quantum Dot Drug Delivery System [46]. The system consists of QD nanoparticles that are soluble in water and therapeutic agents that are able to be entrapped into the structure. The drug release is stimulated and accomplished when sufficient light with specific wavelengths absorbable by the nanoparticle is administered at a close distance to the target site. The ability of the system to respond to specific lights is due to the optical properties that it possesses. Not only that, but the system can also be chemically modified; for example, by implementing polyethylene glycol (PEG) into the structure, the elimination of the nanomedicine by the reticuloendothelial system while circulating in the body can be reduced. This particular alteration allows the nanomedicine to accumulate in the desired site, such as in the tumor cell, and when light with wavelength absorbed by the QD-DDS is administered, the loaded medications can be released from the nanostructure hence enabling its therapeutic effects [47-52].

3. NANOPARTICLES IN CANCER THERAPY

Generally, cancer is well-recognized to be one of the leading causes of death in the world community. By the year 2040, 29.5 million new cancer-related cases and 16.4 million mortalities due to cancer are estimated at a global level [53]. Even though having early interventions such as getting screening tests regularly are excellent choices to improve the disease outcome and increase survival rate, receiving an optimum level of cancer treatments should also be taken into consideration. The desirable therapeutic treatments are those that are effective, efficacious, and tolerable to patients. In this section, the applications of nanotechnology in the treatment of cancer will be further explained in detail with the aid of patents listed in Table 4 below as well as relevant scientific articles to support the respective inventions. The patents listed are classified based on the means of cancer treatment; in this particular review, photodynamic therapy, chemotherapy and radiotherapy will be discussed.

3.1. Nanoparticles in Photodynamic Therapy

A brief description of photodynamic therapy (PDT): it is also known as phototherapy and is one of the many interventions in cancer treatment. PDT is a treatment that utilizes specific drugs, referred to as photosensitizer (PS). The PS will only be activated when light with certain wavelengths is introduced. An excited PS, or activated PS, releases reactive oxygen species (ROS) such as singlet oxygen that can destruct the tumor cells due to its cytotoxic property [54, 55]. Some of the patents relating to inventions that utilize nanotechnology in photodynamic therapy are described in this section.

The patent publication WO2017029501A1 provides information about quantum dot nanoparticles' significance in photodynamic therapy where the particular photosensitizers selected are 5-aminolevulinic acid and its derivatives [56]. The QD nanoparticles can be associated and conjugated with ligands that can target cancerous cells for a better therapeutic effect. On the other hand, US9694074B2 relates to porous silica nanoparticles acting as a transport vector carrying and delivering various photosensitizers that are able to target diseased cells [57]. The desired cell apoptosis is triggered when suitable illumination is introduced. Just like the previous system, the application of silicon-based nanoparticles is used in photodynamic therapy; however, the invention patented (US9592292B1) is explicitly mentioned for the treatment of skin cancer in which the nanomedicine is administered via topical cream [58]. Last but not least, US9616122B2 is associated with pH-sensitive metallic, preferably gold, nanoparticles in phototherapy, where there is a compound conjugated to the nanoparticles’ surface [59]. The charges of the said compound convert or switch when there is a pH change; the compound has a negative charge in neutral or alkaline conditions and changes to positive in acidic environments, like in cancer cells. Significantly, the opposite charges between the positive nanomedicine to the negatively-charged cancer cells allow better binding, thus, enhancing the effect of phototherapy [60].
3.2. Nanoparticles in Chemotherapy

In general, chemotherapy is one of the main interventions for the treatment of cancer. Chemotherapeutic drugs or antineoplastic agents are used in chemotherapy with the primary purpose of killing the cancerous cells. However, in some cases, the chemotherapeutics are administered only to delay the progression of cancer development and to alleviate the cancer symptoms, thus, acting as palliative chemotherapy. Unfortunately, these medications have low selectivity to cancer cells; they are intrinsically toxic to both healthy and abnormal cells. Subsequently, undesirable side effects are observed in patients undergoing chemotherapy owing to healthy tissues being attacked by the potent chemotherapeutic drugs. For that reason, numerous researches are conducted to improve the drug selectivity towards the targeted cancer cells.

The patent US8945629B2 is associated with the invention of polymeric nanoparticles in the application of chemotherapy [61]. The invention helps in rapid delivery of drugs by nanoparticles that have an inner core containing an anticancer drug and a polymer that is soluble in cancer cells. It comprises of a layered nanoparticle system: internal, middle or intermediate, and external layer. The inner core and middle layer consist of varied polymers that will dissolve, particularly in cancer cells' pH, exposing the inner shells and thus releasing the drugs. The chemotherapeutic agent is situated in the inner layer. On the outside layer, water-soluble polymers are present to protect the overall system from being recognized and attacked by the reticuloendothelial system, and prolonging the circulation time of the nanomedicine. It is also feasible for folic acid molecules to be attached at the external layer to improve the absorption of the nanomedicine by cancer cells that have an abundant amount of folate receptors. Therefore, the system advantageously enhances the delivery and uptake of chemotherapeutics to the targeted cancer cells and lengthen the amount of time for the medications to distribute in the body. Another invention patented (US10487207B2) also utilizes polymeric nanoparticles in the application of cancer therapy; the system acts as a nanocarrier that selectively delivers chemotherapeutic agents into the desired target cells due to the sensitivity or specificity to cancer cell environment of the nanoparticles [62].

On the other hand, Bradbury, Yoo, Wiesner, and Ma, (2019) patented (US10485881B2) an invention involving non-mesoporous silica nanoparticles conjugated with chemotherapeutic drugs to detect, prevent, and treat cancer and other diseases [63]. The tyrosine kinase inhibitors such as dasatinib and gefitinib are specifically mentioned in the patent. In essence, the system allows a controllable and predictable release of therapeutic agents to the targeted cancer cells. Whereas the patent US10682421B2 relates to the development of nanoparticle composition capable of particularly targeting cancer stem cells [64]. The system consists of a magnetic iron oxide nanoparticle core serving as a heat source that will enable the release of chemotherapeutic drugs when an alternating magnetic field is introduced, silica nanoparticle to enclose the internal core, and antibodies that allow the system recognize the cancer stem cells.

The next patent, US9662401B2, is associated with developing an invention related to targeting-enhanced anticancer nanoparticles that utilizes serum albumin as the base material for the nanoparticles [59]. The referred albumin supports the passive targeting of tumors by improving the stability of the overall system. Enclosed within the inner core is the appropriate chemotherapeutic agent, and the desired enhanced-targeting effect arises from the porphyrin compound, which is incorporated within the system. Moreover, both albumin and porphyrin enhance the nanomedicine penetration into the tumor cells and increase the accumulated amount of the medications in the targeted site. Consequently, the nanomedicine aims to optimize the delivery of anticancer drugs into the desired tumor or cancer cells, thus, improves the therapeutic effects of the chemotherapy.

Additionally, cancer cells can become resistant to chemotherapeutic agents after being exposed to the medication. The dosages of the drugs are usually increased to overcome this obstacle; unfortunately, this strategy can only work to a certain extent and it brings about more unnecessary and undesirable side effects of the medications. Nevertheless, nanoparticles can be utilized in the treatment of cancer, where the patients have drug resistance to chemotherapeutics. For example, the patent publication WO2017205764A1 describes a nanomedicine composition consisting of double-stranded oligonucleotide and a transport vehicle made up of polypeptides [65]. The chemotherapeutic agents are incorporated with the said oligonucleotide, and then administered into the body. Various tests were also mentioned in the patent to show the effectiveness of the invention in killing the resistant cancer cells, and therefore, essential in treating chemotherapeutic resistance cancer.

3.3. Nanoparticles in Radiation Therapy

Radiation therapy is also one of the means for cancer treatment, where it adopts radiation with high energy to kill the cancer cells; the radiation beams are aimed at a specific and well-defined region of the patient's body. Although the toxic effect of radiation therapy is desirable to attack the cancerous cells, the healthy, normal cells are also exposed to the unwanted risk of radiation therapy. Also, it is probable that cancer tissues develop radiation resistance, resulting in difficulty eradicating the whole tumor; thus, the tumor's relapse is likely [66]. For instance, the patent US9121049B2 demonstrates the application of nanoparticles in radiation therapy [67]. The system is able to distinguish if the cancer cells have radiation-resistance, therefore, ensuring whether radiation therapy is the best choice for the patient. Concurrently, the invention can increase radiation sensitivity in general, including the resistant cancer cells, hence improving the effectiveness of radiation therapy in killing the cancer cells.
Table 4. Relevant patents on cancer therapy mediated by nanoparticles.

| Sr. No. | Patent No. | Classification | Patent/Publication Title | Inventor(s) | Organization | Issue/Publication Date | References |
|---------|------------|----------------|--------------------------|-------------|--------------|------------------------|------------|
| 1       | WO 2017/029501 A1 | (Photodynamic therapy) Based on type of NP: Quantum Dot | 5-Aminolevulinic Acid Conjugated Quantum Dot Nanoparticle | Naasani I | Nanoco Technologies Ltd, GB | Feb. 23, 2017 | [56] |
| 2       | US 9,592,292 B1 | (Photodynamic therapy) Based on type of NP: Silicon | Silicon Nanoparticle for Photodynamic Cancer Treatment Utilizing Quantum Dot Optical Properties | Beckman J, Ischenko A | - | Mar. 14, 2017 | [58] |
| 3       | US 9,694,074 B2 | (Photodynamic therapy) Based on type of NP: Silicon | Functionalized Porous Silicon Nanoparticles and Use Thereof in Photodynamic Therapy | Cunin F, Durand JO, Sailor MJ, Garcia M, Secret E, Gary-Bobo M, Maynadier M, Morea A | Centre National de la Recherche Scientifique (CNRS), FR Universite Montpellier 2 Sciences Et Techniques, FR University of California, US Ecole Nationale Superieure de Chimie de Montpellier, US | Jul. 4, 2017 | [57] |
| 4       | US 9,616,122 B2 | (Photodynamic therapy) Based on type of NP: Metal | pH Sensitive Metal Nanoparticle and Preparation Method | Kim SJ, Jeong SH, Chung HK, Nam JT, Won NY | Postech Academy-Industry Foundation, KR | Apr. 11, 2017 | [59] |
| 5       | US 9,889,212 B2 | (Photodynamic therapy) Based on type of NP: Magnetic metal | Preparation Method for Magnetic Composite for Treating and Diagnosing Cancer | Yang JM, Suh JS, Haam SJ, Lee EG, Hong YC, Ku MH, Heo D, Hwang SY, Huh YM | Industry - Academic Cooperation Foundation, Yonsei University, KR | Feb. 13, 2018 | [68] |
| 6       | US 9,931,410 B2 | (Chemotherapy) Based on type of NP: Polymeric | Nanoparticles for Targeted Delivery of Multiple Therapeutic Agents and Methods of Use | Valencia PM, Pridgen EM, Gadde S, Karnik R, Langer RS, Lippard SJ, Farokhzad OC | The Brigham and Women's Hospital, Inc., US Massachusetts Institute of Technology, US | Apr. 3, 2018 | [69] |
| 7       | US 8,945,629 B2 | (Chemotherapy) Based on type of NP: Polymeric | Nanoparticles for Cytoplasmic Drug Delivery to Cancer Cells | Radosz M, Xu P, Shen Y | University of Wyoming, US | Feb. 3, 2015 | [61] |
| 8       | US 10,487,207 B2 | (Chemotherapy) Based on type of NP: Polymeric | Bioenvironment – Sensitive Nanoparticle Comprising Polymer Having Complementary Charges | Haam S, Huh YM, Kim HO, Choi J, Jang E, Kang B, Noh I, Han S, Song SW, Lee H, Chun H | University - Industry Foundation, Yonsei University, KR | Nov. 26, 2019 | [62] |
| 9       | US 10,335,420 B2 | (Chemotherapy) Based on type of NP: Lipid | Nanoparticle-Based Tumor-Targeted Drug Delivery | Reisfeld RA, Xiang R, Luo Y, Liao D, Liu Z, Chen T, Chen S, Lu D | The Scripps Research Institute, US | Jul. 2, 2019 | [70] |
| 10      | US 10,485,881 B2 | (Chemotherapy) Based on type of NP: Silica | Nanoparticle Drug Conjugates | Bradbury MS, Yoo B, Wiesner U, Ma K | Memorial Sloan Kettering Cancer Center, US Cornell University, US | Nov. 26, 2019 | [63] |

(Table 4 contd....)
| Sr. No. | Patent No. | Classification | Patent/Publication Title | Inventor(s) | Organization | Issue/Publication Date | References |
|--------|------------|----------------|--------------------------|-------------|--------------|------------------------|------------|
| 11     | US 10,682,421 B2 | (Chemotherapy) Based on type of NP: Magnetic metal | Nanoparticle Composition for Use in Targeting Cancer Stem Cells and Method for Treatment of Cancer | Yang M, Liu D | City University of Hong Kong, HK | Jun. 16, 2020 | [64] |
| 12     | US 10,668,151 B2 | (Chemotherapy) Based on type of NP: Albumin-based NP Based on cancer type: Skin cancer | Nanoparticle Complexes of Albumin, Paclitaxel, And Panitumumab For Treatment of Cancer | Markovic SN, Nevala WK | Mayo Foundation for Medical Education and Research, US | Jun. 2, 2020 | [71] |
| 13     | US 9,662,401 B2 | (Chemotherapy) Based on type of NP: Albumin-based NP | Targeting-Enhanced Anticancer Nanoparticles and Preparation Methods of Same | Kim HJ, Hong ST, Chung HJ, Joo MK, Cho HG, Hong J | Jinis Co., Ltd., KR | May 30, 2017 | [72] |
| 14     | WO 2012/131018 A1 | (Chemotherapy) Based on cancer type: Liver cancer | Nanoparticles Loaded with Chemotherapeutic Antitumoral Drug | Pisani E, Lebel-Binay S, Polard V | Bioalliance Pharma | Oct. 4, 2012 | [73] |
| 15     | WO 2012/138013 A1 | (Chemotherapy) Based on type of NP: Polymeric [Drug Resistance] | Paclitaxel-Loaded Polymeric Nanoparticle and Preparation Thereof | Kurt EG, Lee Y | Gwangju Institute of Science and Technology, KR | Oct. 11, 2012 | [74] |
| 16     | WO 2017/205764 A1 | (Chemotherapy) Based on type of NP: Polymeric [Drug Resistance] | Drug-Delivery Nanoparticles and Treatments for Drug-Resistant Cancer | Medina-Kauwe LK | Cedars-Sinai Medical Center, US | Nov. 30, 2017 | [65] |
| 17     | US 9,889,092 B2 | (Chemotherapy) Based on type of NP: Lipid-based NP Based on cancer type: Liver cancer | Low Density Lipoprotein Nanocarriers For Targeted Delivery of Omega-3 Polyunsaturated Fatty Acids to Cancer | Corbin IR | The Board of Regents of the University of Texas System, US | Feb. 13, 2018 | [75] |
| 18     | US 9,415,011 B1 | (Chemotherapy) Based on cancer type: Liver cancer | Method for Treatment of Liver Cancer and Inhibition of Metastasis With CXC-Chemokine-Receptor 4-Targeted Nanoparticle | Chen YC, Liu JY, Gao DY | National Tsinghua University, TW | Aug. 16, 2016 | [76] |
| 19     | US 10,660,861 B2 | (Chemotherapy) Based on cancer type: Pancreatic cancer | Glutaminase Inhibitor Discovery and Nanoparticle - Enhanced Delivery for Cancer Therapy | Hanes J, Slusher BS, Le A, Fu J, Xu Q | The Johns Hopkins University, US | May 26, 2020 | [77] |
| 20     | US 9,121,049 B2 | (Radiation therapy) Based on type of NP: Metal | Pharmaceutical Composition for Elevating Radio-Sensitivity of Cancer Cells, Pharmaceutical Composition for Detecting Cancer Cells with Radio-Sensitivity. And Detection Method Thereof | Shieh DB, Chen HW, Chen CC, Wu PC | National Cheng Kung University, TW | Sep. 1, 2015 | [67] |

4. FDA-APPROVED NANODRUGS

Some of the nanomedicines approved by the United States Food and Drug Administration (FDA) following the year 2010 are summarized in Table 5 below. The nanomedicines’ indication or application, as well as the type of nanoparticle used for each drug, are included in the table. All of the data were collected from the FDA [78, 79].
Table 5. FDA-Approved nanodrugs.

| Drug Product | Manufacturer                      | Type of Nanoparticle/drug | Approved Indications/Applications                              | Approval (Year) | References |
|--------------|-----------------------------------|---------------------------|-----------------------------------------------------------------|-----------------|------------|
| Marqibo      | Talon Therapeutic, Inc            | Liposomal vincristine     | Philadelphia chromosome negative acute lymphoblastic leukemia  | 2012            | [80]       |
|              |                                   | (non-PEGylated)           | (tertiary)                                                      |                 |            |
| Injectafer   | Vifor Inc, Switzerland            | Iron carboxymaltose colloid | Iron deficient anemia                                           | 2013            | [81]       |
| Onivyde      | Merrimack Pharmaceuticals, Inc.    | Liposomal irinotecan      | Metastatic pancreatic cancer (secondary)                        | 2015            | [82]       |
|              |                                   | (PEGylated)               |                                                                 |                 |            |
| VYXEOS       | Jazz Pharmaceuticals               | Liposomal formulation of | Acute myeloid leukemia                                          | 2017            | [78]       |
| (CPX-351)    |                                   | cytarabine-daunorubicin   | (5:1M ratio)                                                    |                 |            |
| ONPATTRO     | Alnylam Pharmaceuticals, Inc       | Lipid nanoparticle RNAi   | Transthyretin (TTR)-mediated amyloidosis                        | 2018            | [83]       |
| (Patisiran)  |                                   | for the knockdown of disease-causing TTR protein |                                                |                 |            |
| Monoferric   | Pharmacosmos                      | Ferric derisomaltose      | Treating iron deficiency and anemia when oral methods do not work or when iron delivery is required immediately | 2020            | [84]       |

Fig. (3). Number of collected patents between 2012 and 2020. (A higher resolution / colour version of this figure is available in the electronic copy of the article).

5. DATA INTERPRETATION

Based on the compiled patents summarized in both Tables 3 and 4, the relationship between the number of patents and the publication year is shown in a bar chart, Fig. (3), for an easy interpretation.

As illustrated from the chart above, the number of patents selected and included in the analysis generally increases, albeit of some consistency in the number of collected patents. This indicates that there is an increment in the relevancy of patents that relate to nanotechnology in drug delivery and cancer therapy throughout the year. Not only that, but it also indicates that there was a growing number of researches being done with respect to nanomedicines, and therefore, more inventions were patented as well. The pie chart displayed in Fig. (4) shows the percentage of collected patents based on the types of nanoparticles included in this review; polymeric, metallic, silicon-based, lipid-based, carbon, quantum dot, albumin-based nanoparticles, and others. It is important to understand that for some inventions that are patented, there is little to no information provided regarding the classifications or types of nanoparticles used. Therefore, these inventions are categorized as ‘others’.
From Fig. (4) above, it can be interpreted that polymeric and metallic nanoparticles are the two most common types of nanoparticles that are utilized in the area of medicine. This is followed by silicon and lipid-based nanoparticles accounting for 13% and 10%, respectively. Conversely, the smallest fractions of the patents are from carbon-based, albumin-based, and quantum dot nanoparticles, with only 5% of the overall patent technologies compiled. The applications of each of the nanoparticle types in drug delivery and cancer therapy have been elaborated in the above sections with the aid of the selected patents.

6. CURRENT & FUTURE DEVELOPMENTS

In this review, the patent literature on numerous different types of nanoparticles applied for the betterment of drug delivery and cancer therapy has been discussed. The types of nanoparticles addressed explicitly in this paper include polymeric, metallic, silica, lipid-based nanoparticles, quantum dots, carbon nanotubes, and albumin-based nanomedicines. Nanotechnology's recognizable advantages urge more substantial interest in conducting studies and inventing systems related to this domain. Also, over the years, it is suggested that there is a noticeable increment in the number of patent applications as well as granted patents, acknowledging the significance of nanotechnology and the relevancy of nanoparticles application in medical practice. From what has been analyzed, the complexity of the pharmaceutical composition is also advancing. With that being said, it is anticipated that more inventions relating to nanomedicines will exist in the near future to provide better therapeutic effects for various diseases, including cancer, improving the patients' quality of life further. However, nanoparticles' potentially toxic effects should also be considered, prompting more research to be carried out.

It is also important to highlight that patenting novel nanotechnology-related innovations and inventions is crucial, especially in healthcare medicines. Due to the risky and high-priced development of drugs in the pharmaceutical industry, drug companies need to file patents to protect their inventions from being illegitimately used by other inventors. It is through patent protection that drug manufacturers can obtain adequate profits and earnings to deal with the expensive research and developments accompanying the process in drug development, thus allowing new medications to be feasibly manufactured in the future.

CONCLUSION

From the literature, it is quite indisputable that nanotechnology contributes significantly to the field of medicine. A plethora of nanoparticle-based inventions have been developed and patented in the application of drug delivery and cancer therapy. The growing number of patent technologies in these particular areas of medicine may be due to the numerous and diverse advantages that nanoparticles provide; not only can they improve the bioavailability and solubility of certain therapeutic agents, but also, they can enhance the drugs' stability and prolong the release of medications. Moreover, due to their small dimensions, it is feasible for the nanomedicine to penetrate the blood-brain barrier, plus they can also protect the medications from being physiologically degraded. In terms of cancer therapy, remarkably, nanotech-
nology can better target cancer cells and provide benefits in chemoresistant cancer treatment. Ultimately, this review has come to the conclusion that the utilization of nanoparticles in medicines is essential in the pursuit of better clinical practice. Nonetheless, it is crucial to recognize and understand the concerns relating to nanomedicines’ safety, biocompatibility, and toxicity.

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CONFLICT OF INTEREST

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