

Biosensors Enhanced with Nano-Silica in Cancer Detection

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Abstract:

Nano-silica is a versatile material, which is cost-efficient, non-toxic and abundant in nature. This material is effectively used for diagnosing cancer. Point-of-care devices are portable, user-friendly, highly accurate and capable of real-time detection. Point-of-care devices like biosensors incorporating silica nanoparticles demonstrate remarkable specificity and selectivity in cancer diagnosis. Types of cancer include blood cancer, ovarian cancer, cervical cancer, breast cancer, skin cancer, prostate cancer, etc. Detecting cancer in human cells and tissues is by the presence of appropriate cancer biomarkers. In this article, a systematic review is presented on the history and classification of silica nanoparticles. Special attention is given to their role in sensors and imaging, while silica nanoparticles contribute to enhanced sensitivity and reliability. This review further explores how silica nanoparticles are efficient in diagnosis of cancer. Additionally, it discusses diverse cancer biomarkers that aid in identifying cancer types, thereby contributing to improved early diagnosis and targeted treatment strategies.

Keywords: Cancer; Silica; Biosensors; Biomarkers point-of-care devices

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1. Introduction:

Cancer is one of the major causes of death worldwide, which is increasing sharply. Chemotherapy is the traditional method used in treating cancer, but it has certain limitations like it could affect normal healthy cells along with tumor cells, the radiation could cause subsequent complications including damage to the DNA, there are chances for the recurring of the disease and withstand therapy proving it less efficient. “Targeted drug delivery” is crucial to overcome limitations of conventional chemotherapy [1]. In addition to chemotherapy, tumor cells are removed surgically, or by radiation therapy or hormone-related therapy, each are successful towards cancer treatment at the same time less efficient in the view of specificity and selectivity [2].

Ligand-specific delivery systems are used to selectively bind to target site without causing any damage to surrounding sites. Lipid nanoparticle is also highly selective and specific to target tumor cells [3]. Cancer stem cells which are sub-groups of tumor cells are able to cause recurrent tumor. These cells are resistant to chemotherapeutic agents which cause the cells to rapidly multiply and withstand anti-cancer drugs [4]. Continuous growth of tumor lesions affects tissues and finally organs which are severe threats to human life. Cancer can affect any important part of the human body including lungs, liver, bones, blood and the brain [5]. Cancer cells are typically identified by the presence of biomarkers, which are specific to each type of cancer. These biomarkers help in early diagnosis of disease, thus improving the quality of life [6]. Cancer treatment is targeted towards inhibition of biomarkers which are biological molecules like genes, proteins or peptides used in identifying tumor cells [7]. To overcome the limitations of conventional cancer treatment methods,

integration with nanomaterials could help. Due to the extremely small size of nanoparticles, they are capable of passing through tiny blood vessels and capillaries to selectively bind to cancerous cells and engulf them. Controlled drug release is possible for several weeks or months with ensured safety by using biocompatible materials in preparing nanomaterials. Different nanomaterials like carbon-based, metals and metal oxides, inorganic nanomaterials, polymeric and lipid nanoparticles are used in cancer diagnosis [8]. Silica nanoparticles are mainly used in diagnosing breast cancer due to its efficiency as a drug carrier [9]. Its inherent properties such as tunable particle size, less density, high drug loading efficiency have proved “core-shell” mesoporous silica as efficient candidates for “drug delivery” [10]. One dimensional form of silica is used in identifying “microRNA” which is a specific biomarker for breast cancer [11]. Silica is used in diagnosing prostate cancer, which is a common type of cancer in men [12]. An anti-cancer drug named “Docetaxel” is used in detecting prostate cancer cells [13]. Mesoporous silica was loaded with a drug called “Enzalutamide” along with folic acid, and used in prostate cancer diagnosis and treatment [14]. Core-shell mesoporous silica when coated with lipid and “Cabazitaxel” anti-cancer drug shows enhanced biocompatibility and cytotoxic effect against PC3 prostate cancer biomarker [15]. Mesoporous silica is also used in diagnosis and treatment of cervical and ovarian cancer using “5-Fluorouracil” anti-cancer drug [16]. Mesoporous silica with high porosity functionalized with folic acid is used in diagnosis of cervical cancer cells [17]. In addition, skin cancer “Melanoma” is diagnosed by mesoporous silica [18]. Enhanced cytotoxic effect to melanoma cells were found when silica is loaded with drugs like “Curcumin” and “Quercetin” [19].

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Table 1. Three major cancer types affecting men and women in the year 2022

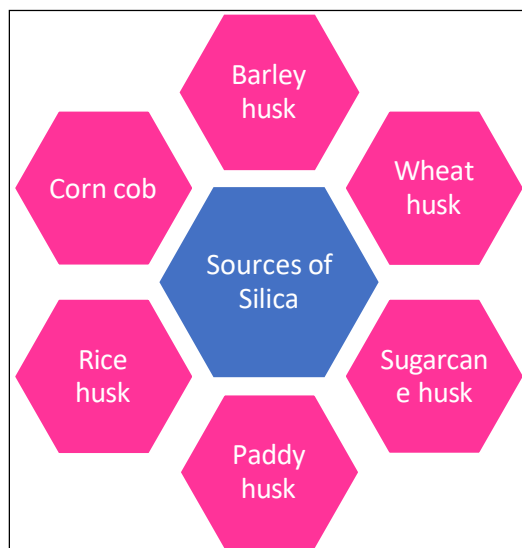
Cancer caused in Men	No. of cases	No. of deaths	Reference
1. Prostate cancer	1,466,680	396,792	[20,21]
2. Lung cancer	1,571,868	1,233,109	
3. Liver cancer	600,243	521,433	
Cancers caused in Women	No. of cases	No. of deaths	Reference
1. Breast cancer	2,295,686	665,684	[20,21]
2. Cervical cancer	661,021	348,189	
3. Lung cancer	908,433	584,063	

Table 2. Top cancer prevailing countries and their statistics in 2020

Cancer incidence in Males:		Cancer deaths in Males:		Reference
No. of cases (per 100,000)	Country	No. of cases (per 100,000)	Country	[21]
494.2	Western Africa	165.6	Eastern Europe	
100.6	Australia/New Zealand	70.2	Central America	
Cancer incidence in Females:		Cancer deaths in Females:		Reference
No. of cases (per 100,000)	Country	No. of cases (per 100,000)	Country	[21]
405.2	Australia/New Zealand	118.3	Melanesia	
102.5	South Central Asia	63.1	Central America	

2. Silica nanoparticles:

Silica is prepared from “chemical” and “biogenic” methods. Figure 1 shows the production of silica from various agricultural sources [22].

**Figure 1. Agricultural Sources of Nano-Silica**

The advantages of mesoporous silica nanoparticle is that its pore size, diameter of particles and its porosity can be tuned for specific applications. For biomedical applications, one-dimensional nanoparticles with a size range of 10-300 nm are appropriate. Mesoporous silica comes in a variety of porous shapes. Figure 2 shows the porous shapes of mesoporous silica [23].

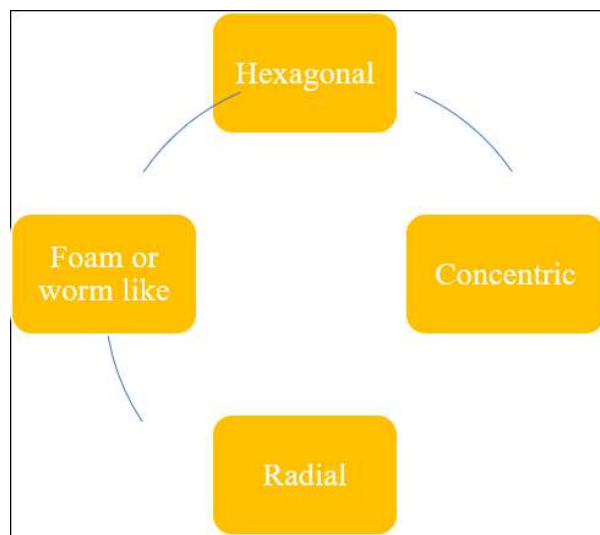


Figure 2. Porous shapes of Mesoporous silica

2.1 History and Development: (Only Silica) – who first invented Nano silica

A brief chronological order of the evolution of silica nanoparticles is shown in figure 3 [24–27].

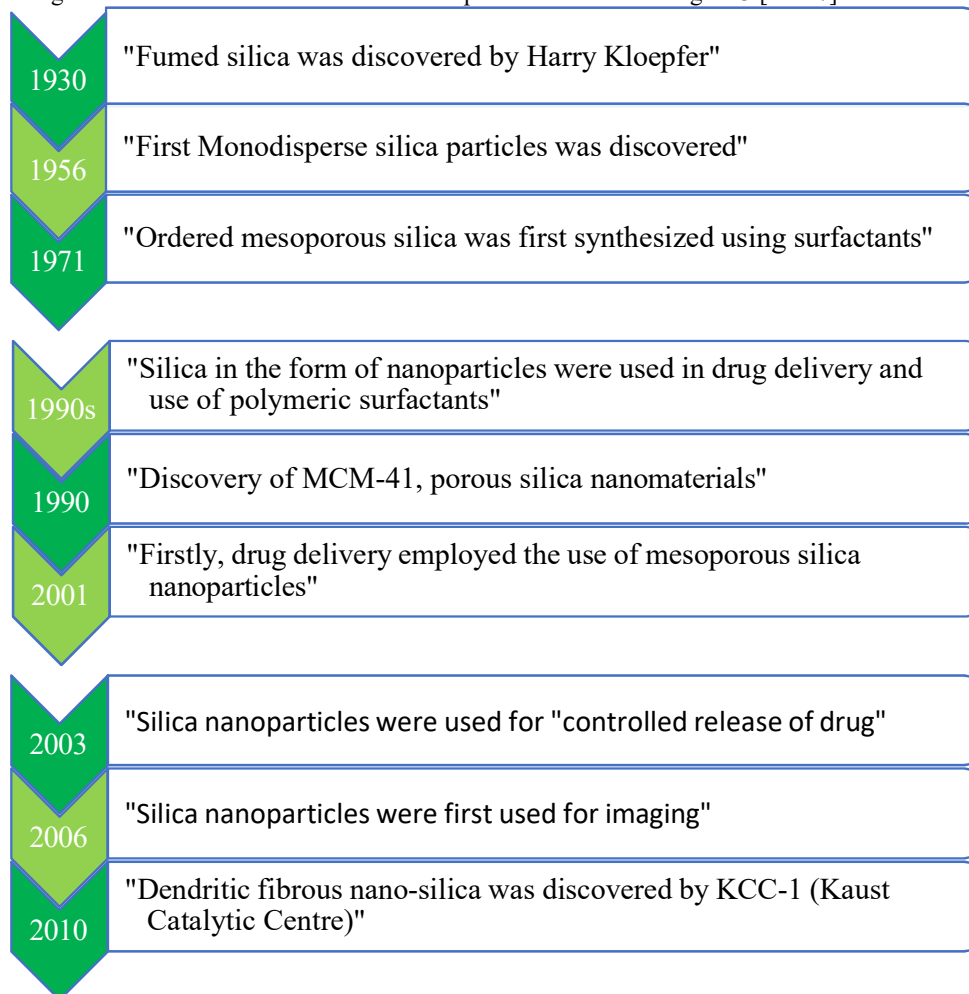


Figure 3. History of silica nanoparticles

2.2 Classification of silica based on phase or structure:

Silica nanoparticles are broadly classified into:

(i) Mesoporous silica nanoparticles

Has a porous structure with large pore volume

(ii) Solid silica nanoparticles

Has a non-porous structure and useful for biomedical applications [28].

Based on pore diameter, porous nanostructures are classified into three types.

(i) Microporous – less than 2 nm

(ii) Mesoporous – between 2 to 50 nm

(iii) Macroporous – more than 50 nm [28].

Silica exists in porous and non-porous forms:

POROUS SILICA	NON-POROUS SILICA	REFERENCE
- Has unique pore structure - Suitable for application in medical field - Specifically used in drug delivery, diagnosis and therapy.	- Has no unique pore structure - Biocompatible in nature - Due to its structure, not suitable for biomedical field	[29]

Table 3. Differences between porous and non-porous types of silica (SiO₂)

2.3 Quantum Confinement effect of nano-silica:

Due to quantum confinement effect, the size of nanocrystal decreases but there is an increase in band gap. Silicon quantum dots have pronounced effects in “biomedical tagging” [30]. The nanostructures that exhibit quantum confinement effect are nothing but “Quantum Dots”. For quantum dots of size 1 nm, the strain and energy gap decreases, which is reverse for 2 nm size quantum dots [31]. Quantum dots, mesoporous silica nanoparticles are biocompatible in nature, so used in biomedical imaging, cancer diagnosis and treatment [32].

improve its efficiency in such point-of-care devices [37]. Mesoporous silica along with ruthenium is used in “Electrochemiluminescence”, a point-of-care device to identify “Severe-Acute-Respiratory Syndrome”, a

3. Mesoporous Silica Nanoparticles in POC devices:

Silica nanoparticles are used in Electrochemical biosensors for detection Escherichia Coli bacteria, with a detection limit of 2×10^3 CFU/ml (colony forming unit/millilitre). Mesoporous silica is used in calorimetric and fluorescence biosensors for detecting Salmonella Typhimurium, typhoid-causing bacteria, with detection limit of 63 CFU/ml and 40 CFU/ml respectively [33]. Optical biosensors use porous silicon for detecting biological units like “DNA, enzymes, cells, bacteria and antigen”. Optical biosensors fabricated using porous silicon is used in diagnosing cancer. For example, it can detect heat shock protein 70, to identify several types of cancer [34]. “Porous silicon biosensor was fabricated to detect Escherichia Coli bacteria with 10^1 to 10^2 CFU/ml limit. Mesoporous silica combined with other metal oxides or carbon nanomaterials are used in early identification of bacterial infections with high accuracy [35]. Porous silicon when coated with carbon used in designing Glucose Sensor which helps identify “Glucose dehydrogenase” and Glucose oxidase” [36]. Mesoporous silica is used in “Microfluidic devices” to detect presence of infections caused by Helicobacter pylori and Hepatitis A by scanning a blood drop and detects glucose and urea from sweat. Cotton threads which are cheap raw material is coated with silica to

ratory disease with a range of $1 - 10^4$ ng/ml with 52 ng/ml as detection limit [38]. CRP protein is detected by using silica coated with fluorescent materials. Silica with quantum dots increase its performance, thus mesoporous silica is used efficiently sensing devices which is advantageous due to its low cost and zero toxicity [39].

4. Metal oxides in Nano-silica POC devices:

4.1 Titanium dioxide:

Titanium dioxide (TiO_2) based nanocomposites have attracted a rising interest as functional materials for biosensor applications. Biosensors based on TiO_2 are used in electrochemical, optical, electrochemiluminescence biosensors [40].

4.2 Tin oxide:

Tin oxide along with mesoporous silica is used in sensing “volatile organic compounds” which detects diseases such as gingivitis, oral carcinoma, periodontal diseases and diabetes mellitus. [41].

4.3 Copper oxide:

Copper oxide nanoparticles possess significant intrinsic properties which are suitable for cancer diagnosis and treatment. Nanorods of copper oxide are used in detecting and destroying tumor cells causing breast cancer without any disruption to normal healthy cells [42].

4.4 Zinc oxide:

Silica prepared by green synthesis, when coated with zinc oxide, has increased efficiency to combat bacterial infections caused by *Staphylococcus*, *Escherichia coli* and *Pseudomonas* [43].

4.5 Iron oxide:

These metal oxides have improved magnetic properties, so proven to be used in bio-imaging of cancer cells. Ovarian cancer is identified and treated by targeted drug delivery using iron oxide nanoparticles [44]. Iron oxide is synthesized in environment friendly plant-based approaches which are effective in diagnosing and treating cancer cells in human body [45].

5. **Biosensors:** A biosensor uses electrical, thermal and optical signals to detect diseases in tissues, cells, enzymes and immune system [46]. In 1960, the first biosensor was discovered by “Leland C. Clark Jr.” to detect amount of glucose in diabetes patients [47]. Diseases like cancer are quickly diagnosed and treated using biosensors [48]. Modern technologies include biosensors that are wearable to enable people to assess health information any moment, at any location [49]. A biosensor uses electrical, thermal and optical signals to detect diseases in tissues, cells, enzymes and immune system [50].

The advantages of biosensors include,

- Simplicity
- Flexibility
- Accuracy
- Specificity

- High speed and
- Cost effectiveness [47].

The broad classification of biosensors include:

- Electrochemical biosensors
- Optical biosensors
- Piezoelectric biosensors
- Fluorescent biosensors and
- Thermometric biosensors [51]. Capillaries are a type of point-of-care devices that are used in biosensors for detecting proteins, carbohydrates, lipids and nucleic acids [52]. A typical biosensor consists of four stages
 - (i) **Biological recognition element:** - Interacts with blood and bodily fluids
 - (ii) **Transducer:** - Converts the interaction into signal
 - (iii) **Signal processor:** - Converts biological signal into electrical signal
 - (iv) **Reader:** - Displays the output [53].

Biosensor in the form of paper can be strips on which blood samples and other body fluids are tested, whereas chip-sized biosensors are made up of “Polydimethylsiloxane - PDMS”, both are used in immediate and accurate detection of infectious diseases [54].

The four main types of Electrochemical biosensors used in detecting analytes in the human body are as follows:

- Conductometric
- Potentiometric
- Voltammetric
- Amperometric [48]

Figure 4 lists the biosensors used in three different types of cancer identification [55].

Figure 4. Biosensors used to detect three main types of Cancer With the increasing risk of cancer which originates in a cell or tissue and

Lung cancer	Pancreatic cancer	Breast cancer
Fluorescence-based biosensors	- Electrochemical biosensors - Plasmonic-based biosensors	Biosensors with Surface Enhanced Raman Spectroscopy

multiples affecting other cells and organs of

the body and pose a severe threat, nanomaterials play a significant role in early diagnosis and treatment of cancer due to its advanced properties [56].

5.1 Nano-silica in Biosensors:

The stability of biosensors is due to factors like, temperature, pH and conditions for storage. Nanomaterials like mesoporous silica can better enhance thermal and chemical stability which are efficient than polymeric and organic materials that are used in conventional biosensors. Further when quantum dots are used in biosensors, it is used to detect cardiac biomarkers [57]. The main advantage of using silica is its flexible mechanical, optical, thermal and physical properties, adjustable pore size, biocompatibility and biodegradability which are used effectively for biomedical applications such as drug delivery, imaging and sensors [58]. Biosensors play a vital role

electrochemical biosensors due to its advantages such as rapid response, sensitivity, accuracy and stability. These compact devices are used point-of-care diagnostics [61].

Biomarkers – its types for cancer cells:

The classification of biomarkers that are used in detecting cancer

in identifying cancer by detecting specific biomarkers, glucose levels, and several diseases. Inorganic nanomaterials, carbon-based nanomaterials and organic nanomaterials lesser than 500 nm is used in enhancing the efficiency of biosensors [59]. Nanoscale materials in the form of tubes, rods, wires and particles at size 1-100 nm is used in biosensors for precise detection of biomolecules (Narware et al. 2025).

Combination of different nanomaterials like polymers, metal nanoparticles and carbon-based materials are proved to improve the stability, accuracy and sensitivity of biosensors. Biosensors provide digital output by analyzing different biomolecules. Due to its advantages, it is ideal for point-of-care diagnostics [60]. Biosensors are divided into number of groups according to the physical principles and processing technique employed Optical biosensors are highly efficient than

(i) Diagnostic biomarkers:

Identifies disorders when they occur

(ii) Prognostic biomarkers:

Offer information about a patient's total intended clinical progress

(iii) Predictive biomarkers:

Determine the general intended clinical result [62,63].

Table 4. Different biomarkers used in identifying types of cancer

TYPES OF CANCER	TYPES OF BIO-MARKERS	REFERENCE
1. Breast cancer	ER, PR, HER2 and Ki-67	[64]
2. Lung cancer	EGFR, ALK, ROS1, MET, HER2	[65,66]
3. Prostate cancer	PSA, PCA3, Prolaris, ProMark, PHI	[67]
4. Ovarian cancer	CA-125, HE4, BRCA1/2, FGF	[68]
5. Gastric cancer	CEA, CA72-4, CA19-9, CA125	
6. Endometrial cancer	PTEN, TPS, HE4, E-cadherin	
7. Pancreatic cancer	CA19-9, CEA, CA125, CA50	[69]
8. Cervical cancer	CCR7, CD3D, ITGB2, TP53	[70]
9. Liver cancer	AFU, DCP, AFP, GP73	[71]
10. Colorectal cancer	CEA, EGFR, KRAS, MSI	[72]

6. Conclusion:

Nano-silica emerges as a highly promising material in the biomedical field, particularly in the development of advanced biosensors and cancer diagnostic tools. Its inherent features such as biocompatibility, low toxicity, cost-effectiveness and structural versatility, make it an ideal candidate for integration into point-of-care technologies. When combined with other functional materials, silica nanoparticles significantly enhance the sensitivity, specificity and reliability of biosensors, enabling the rapid detection of a wide range of biomarkers. Such improvements hold particular value in early cancer detection, where accuracy and timeliness are crucial. Beyond diagnosis, the adaptability of nano-silica paves the way for personalized medical applications and next-generation healthcare systems. With ongoing advancements in nanotechnology, the use of silica nanoparticles is expected to revolutionize biosensing platforms and transform point-of-care testing, thus this material is excellent choice for biomedical applications.

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