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REVIEW ARTICLE

Recent advances in nanomaterials integrated immunosensors for food toxin detection

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Abstract For the management and prevention of many chronic and acute diseases, the rapid quantification of toxicity in food and feed products have become a significant concern. Technology advancements in the area of biosensors, bioelectronics, miniaturization techniques, and microfluidics have shown a significant impact than conventional methods which have given a boost to improve the sensing performance towards food analyte detection. In this article, recent literature of Aflatoxin B_1 (AFB_1), worldwide permissible limits, major outbreaks and severe impact on healthy life have been discussed. An improvement achieved in detection range, limit of detection, shelf-life of the biosensor by integrated dimensional nanomaterials such as zero-dimension, one-dimension and two-dimension for AFB_1 detection using electrical and optical transduction mechanism has been summarized. A critical overview of the latest trends using paper-based and micro-spotted array integrated with the anisotropic shape of nanomaterials, portable microfluidic devices have also been described together with future perspectives for further advancements.

Keywords Food toxins · Aflatoxin B_1 · Biosensors · Nanomaterials · Electrochemical transduction · Optical transduction

Introduction

Foodborne illness is one of the significant worldwide issues that shows several adverse impacts on travel, trade, and development (Käferstein et al. 1997). The primary cause of foodborne illness is the consumption of food that contains unhealthy microorganisms, including infectious bacteria, viruses, parasites, fungus, and non-infectious chemicals or toxins (Neethirajan et al. 2018). This problem is still not under control, and outbreaks can cause an economic loss of billions of dollars (Luo et al. 2018). The global statistical estimation indicates that about 48 million people get affected and about 0.12 million are admitted to the hospital every year due to the food toxins (Das et al. 2017). Four categories are prominently known through which food illness may spread from farm to forks such as plant toxin, a bacterial pathogen, phycotoxin, and mycotoxin (Malhotra et al. 2014). Plant toxin is a secondary metabolite produced by the plant, especially to defend themselves from various threats such as bacteria, fungi, insects (Mithöfer and Maffei 2016). Some harmful chemicals are present like terpenoids, alkaloids, phenolic groups, and toxin like Ricin, which is a lectin (carbohydrate-binding protein) naturally found in castor beans, red kidney beans, white kidney beans, bamboo shoots and flaxseed, cyanogenic glycosides in bitter apricot seed, muscarine in wild mushrooms, and in many more (Mithöfer and Maffei 2016). Ingestion of toxic chemicals like cyanide and alkaloids into the human body show toxicological effects from acute to chronic which can lead to the death of a person. Another severe

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microorganism is Pathogenic bacteria, which is also known as harmful bacteria. *Mycobacterium tuberculosis* is one of the well-known bacterial pathogens causes tuberculosis (Doss et al. 2017) and about 2 million people in a year get affected especially in sub-Saharan Africa and Asia region (Seale et al. 2014) cause severe infections such as typhoid fever, syphilis, tetanus into the human body. Another toxin which found in the form of Phycotoxin is a complex allelopathic toxic chemical substance that can be prokaryotic and eukaryotic algal secondary metabolites produced by marine microalgae (Rasmussen et al. 2016).

Another most common toxin present in a wide variety of food and feedstuffs is Mycotoxin, a secondary metabolite produced by the fungus, found in almost all agricultural commodities such as coffee, cereals, wine, maize, corns, groundnuts, rice, meat, flour, almonds (Adeyeye 2016). Regional, seasonal, and year-to-year climate variability and global warming strongly affects agricultural food production, especially in some particular regions such as tropical and subtropic areas of the world. Mycotoxins growth occurs by either field fungi that grows in the field known as pre-harvest, and other is the storage fungi typically occur after harvest known as post-harvest (Torres et al. 2014). During pre-harvesting and harvesting, few factors such as temperature, gas composition, pH, chemical additives, moisture, water stress and insect damage affect the rapid fungal growth including Aflatoxin growth in food crops. During the rainy season, unusually hot and dry conditions are responsible for the growth of *Aspergillus* and *Paramecium* species, which continue to grow and produce till the transport and storage take place. Over 40 known mycotoxins, most common include Aflatoxins, Ochratoxin A, Fumonisin, Citrinin, T2-Toxin, Zearalenone, Ergot alkaloids, deoxynivalenol, etc. (Hajslova et al. 2011).

Among the classified class of mycotoxin, series of Aflatoxins such as B_1, G_1, B_2, and G_2 are known to be hazardous food toxins. The chemical structure of the AFG series differs from the B series by the replacement of β-lactone groups to cyclopentanone (Jaimez et al. 2000). Also, the B series of Aflatoxins produces a blue fluorescence, while G-series produces a green under ultraviolet radiation; however, AFM_1 produces blue-violet fluorescence, and M_2 produces only violet fluorescence at 365 nm. Thus, these Aflatoxins series have distinguished chemical groups that emit their respective fluorescence colors under the ultraviolet radiation. In addition to this, the toxic effects of potency is followed in the order of AFB_1 $> AFG_1 > AFB_2 > AFG_2$ (Chen and Inbaraj 2016).

AFB_1 is the most potent toxic mycotoxin, which is primarily produced by molds or multiple strains of *Aspergillus Flavus,* and *Aspergillus Parasiticus* grows in agricultural commodities as well as in multiple staple foods (Kabak and Dobson 2015). AFB_1, potent of carcinogen, contains a chemical composition of furocoumarin cyclopentanone and lactone moiety. When AFB_1 is inhaled, ingested, or absorbed through the skin, responsible for carcinogenic, teratogenic, mutagenic effects in humans and animals (Afsah-Hejri et al. 2013). It produces in various grains and nuts, such as in peanuts, cotton, cocoa, coffee beans, medical herbs, corns, wheat, maize, rice, pistachio, grains, spices. Some crops like maize and groundnut products are considered as a main component of the human diet and even crucial to human survival. However, in the late 1990s, globally, but especially in India, maize and peanuts were considered as a major source of aflatoxin (Shekhar et al. 2018). Even economically, they show adverse effects by reducing the yield of fiber crops and approximately 6 billion people worldwide exposed to aflatoxin in the human diet (Oranusi et al. 2017). According to Food and Agricultural Organization of United Nations, about 25% of the food crops around the entire world spattered with mycotoxin which is a significant economic loss (1000 million metric tons per year) (Oranusi et al. 2017) therefore reduces the supply of food and feedstuffs from farm to fork consumer consumption. The statistical estimate indicates that out of 76 countries, 63 countries have an impact of aflatoxins in their food contents (Khlangwiset et al. 2011). Eventually, there is a strict official regulation for mycotoxins consumption in food products that have been shared globally with National and International organizational.

The production of AFB_1 in crops, consumption by a human being as well as by animals, along with their biological transformation into human and animal bodies by adduct formation with DNA and protein, lead to creating several acute and chronic diseases as described schematically in Fig. 1.

Aflatoxin was first discovered in the 1960s had an outbreak of disease, Turkey-X in London, England (Scott 1978). Turkey-X disease was responsible for 0.1 million turkey poult, duckling, and chick death because of the consumption of peanut meal contaminated with fungi *Aspergillus flavus* and present toxin as aflatoxin. Moreover, in 1974, in the states of Rajasthan and Gujarat in India, 106 people were died due to the consumption of Aflatoxin (Reddy and Raghavender 2007). In 1985, the rate of egg production dropped from 85 to 50% in India because of the high impact of severe aflatoxicosis, which was toxic hepatitis led to jaundice in poultry. Also, in 1994, 0.2 million broiler chickens died in the state of Andhra Pradesh in India due to the consumption of Aflatoxins contaminated groundnut feed in their food products (Reddy and Raghavender 2007). The impact of Aflatoxin has also been increased in European countries from low to medium probability, where maize cultivation very common. Another major outbreak of acute aflatoxicosis was

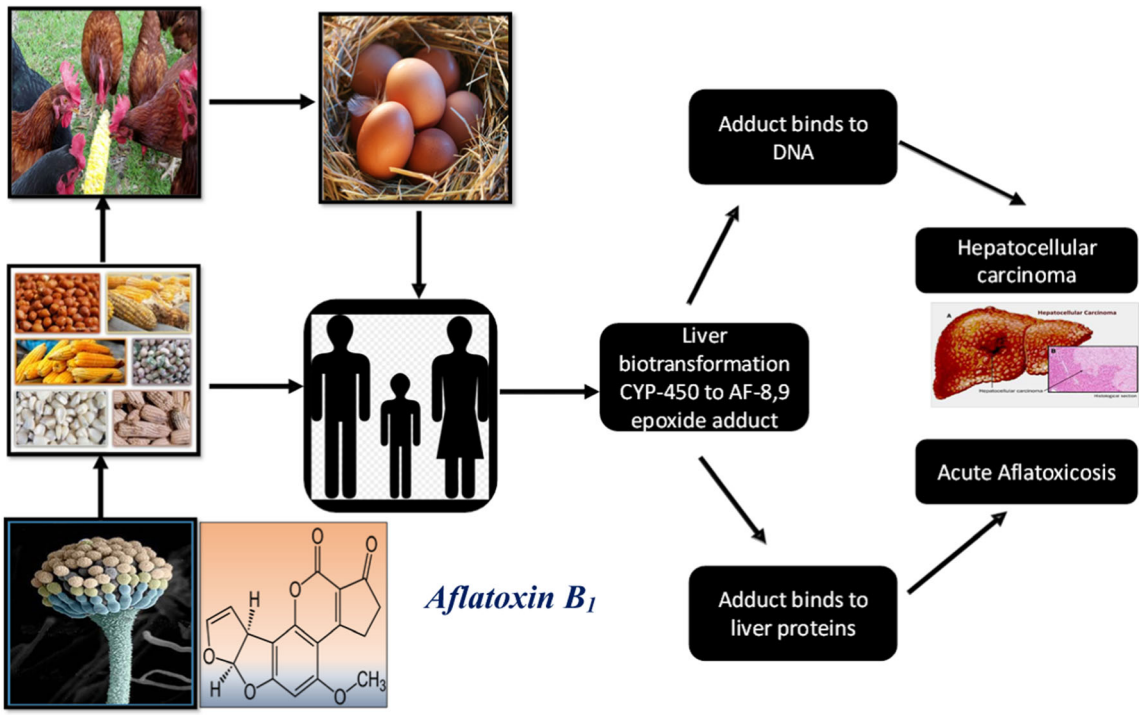

Fig. 1 Overview of AFB_1 with harmful effects on human health

observed in the eastern part of Kenya in 2004, where 500 cases of acute aflatoxicosis have come out along with 184 deaths of people (Tefera et al. 2011).

In almost 100 countries, National, as well as International Organizations and agencies, have set universal standardization for the consumption of mycotoxins in daily diet food products. Some of them set standards for total Aflatoxins (B_1, B_2, G_1, and G_2) and AFB_1, while some of them established a maximum tolerance level only for AFB_1 in food (Fig. 2). However, the European Union (EU) set a maximum permitted limit of AFB_1 to 2 μg/kg and for total Aflatoxins to 5 μg/kg, commonly present in maize, cereals, groundnut, dried fruits, and species while the maximum allowance of AFB_1 and M_1 in infant food to 0.025 μg/kg (Zinedine and Mañes 2009). Similarly, European pharmacopeia had implemented strict regulations for AFB_1 in foods, and the allowed limit to 2 μg/kg, and the total Aflatoxin limit to 4 μg/kg in foodstuffs for direct consumption (Zinedine and Mañes 2009). According to Indian Food Safety and Standard Regulation, the maximum permissible limit of Aflatoxins (B_1, B_2, G_1, and G_2) content in all food commodities to 30 μg/kg, while the tolerance value for AFM_1 in milk to 0.5 μg/kg for sale in the Indian market (Reddy et al. 2010). Moreover, according to the United States of Food and Drugs Administration (FDA), 20 μg/kg is a specific limit for consumption of toxicity in food (Aquino and Corrêa 2011; Nishimwe et al. 2017). AFB_1 is responsible for the sixth most leading liver cancer throughout the World, and it is classified as Group-I carcinogen by the International Agency for Research on Cancer (IARC) (Nishimwe et al. 2017). In developing countries, 600,000 new cases per year have been found because of the consumption of contaminated food (Ozakyol 2017). Moreover, according to the World Health Organization (WHO), AFB_1 is responsible for liver cancer, kidney failure, and reduced efficiency of the immunological system.

Malhotra et al. have reviewed the applications of nanomaterials based biosensor for food toxin detection and also on carbon nanotubes-graphene based biosensor for food toxin detection exclusively utilizing carbon nanomaterials for the electrochemical biosensor for mycotoxins detection (Malhotra et al. 2014, 2015). These involve overview about the utilization of graphene, fullerenes, carbon nanotubes and their derivatives for the fabrication of electrochemical biosensor for AFB_1 detection. Improvement in the electrochemical bioanalytical performances of the device has also been briefly described along with the merits and prospects of the biosensor. Similarly, Bunney et al. published a review article on the use of electrochemical biosensor in food analysis (Bunney et al. 2017). This review article is basically focused on the food safety, biosensor attributes, new leap in biosensing and food analysis challenges over the conventional techniques available. Main discussion has been made on the food analysis and biosensor based quantification. Similarly, Yan

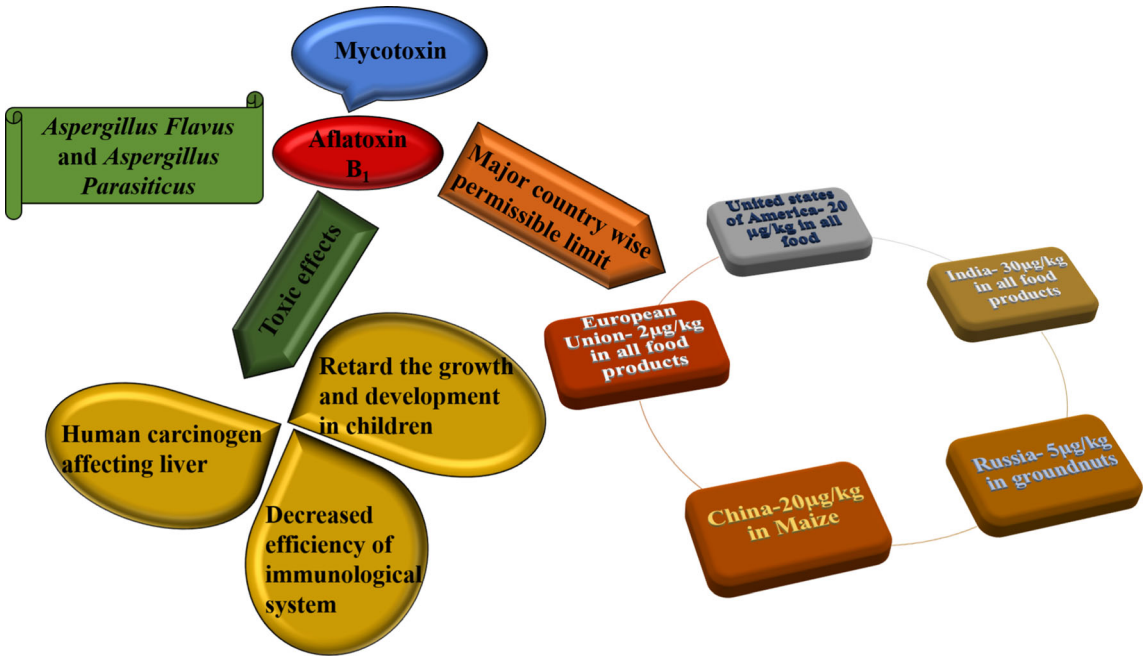

Fig. 2 AFB_1 effects and permissible limit in food products

et al. reported a review article on the recent advances in aflatoxins detection based on nanomaterials (Yan et al. 2020). Basic aspects about the toxicity, significance of aflatoxin detection, development of metal oxide and hydroxide, carbon based nanomaterials integrated biosensor have been discussed.

The present review article is mainly focused upon the depth description about the food toxin, mycotoxins, AFB_1 detection and nano-biosensor devices, country wise permissible limits of AFB_1 and the biosensing characteristics are categorized based on the dimension of nanomaterials. Role of the nanomaterials and recent advancement using microfluidic devices are also highlighted in the present review. Besides this, the review article is structurally organized highlighting the recent works on the fabrication of immunosensors with respect to dimension based nanomaterials, their properties, and application in the fabrication of optical biosensors such as Surface Plasmon Resonance and Fluorescence biosensor as well as electrochemical biosensors for food toxin detection have been summarized. Also, recent trends in paper-based and microspotted array microfluidic biosensor with anisotropic shape of nanomaterials have been discussed and last few years published works using microfluidic technique for food toxin detection have been summarized together with future perspectives for further advancements.

Conventional techniques available for AFB_1 detection

In terms of safety concerns, a sophisticated tool should be available to quantify the content of AFB_1 in food. Due to its potential hazardous towards the life of humans and animals, detection entirely becomes important in controlling economic losses, infections in crops, and various health issues. Numerous conventional techniques are available for their detection such as Thin Layer Chromatography (TLC), High-Pressure Liquid Chromatography (HPLC), Gas Chromatography (GC)-Mass Spectroscopy (MS), ultraviolet absorption, fluorescence technique, etc. being used in the testing laboratories for the detection of AFB_1 (Fig. 3). Although, TLC and HPLC are well established conventional technique for qualitative analysis of food content due to the precise and accurate detection results but these instruments are highly expensive, even well-equipped laboratory needed, trained personnel required for the analysis, harmful chemicals used during the experimental procedure, and followed a tedious procedure are the certain limitations. These techniques take a long time for the analysis of samples, which is unsuitable for testing of many samples. Liquid-chromatography coupled with Mass spectroscopy is also advanced analytical technique for simultaneous mycotoxins determination. AFs, T-2 toxin, Fumonisin can quantify by using reversed phase solid-phase extraction column for extra cleanup (Singh et al. 2020). Also, more advanced column such as liquid–liquid, accelerated solvent extraction, solid-phase

Technique	Advantages	Limitations
Thin-layer chromatography	Visual estimation, Simple, Inexpensive,	Poor sensitivity, poor precision, low repeatability, screening results are ambiguous, low level of automation
High-performance Liquid chromatography	Good sensitivity, good selectivity, automated, high fluorescence intensity	Expensive equipment, need expertise, weak absorption of UV-radiation, derivatization required
Enzyme-linked immunosorbent assay	Simple sample preparation, inexpensive equipment, suitable for screening, visual assessment	Cross reactivity, matrix interference problem, possible false –ve/+ve results semi-quantitative, high cost per sample due to low specificity and colour change
Immunosensor	User-friendly, Rapid, cost-effective, good selectivity, sensitivity, portable, used for multiple mycotoxins detection, suitable for screening	Selection of suitable immobilizing matrix and technique is crucial to optimize best electrochemical parameter to obtain enhance biosensing performance (sensitivity, selectivity, detection limit, stability)

Fig. 3 Comparision chart between conventional techniques and Immunosensor for food sample detection

matric dispersion are highly useful, and their aim is to reduce the matric effect as much as possible by minimizing the interference effect. Major limitation of LC–MS often gives unsatisfactory results for quantitative measurement of mycotoxins due to ion suppression and matrice effects (Singh and Mehta 2020). However, another promising technology has been explored using the fluoroimmunoassay strategy. For example, Enzyme-Linked Immunosorbent Assay (ELISA) has come into consideration of analytical practice. In the past few years, several studies have been conducted using this method, but the label-based test system needs a specific marker, which often requires long waiting time for labeling, a large amount of analyte, cross-reactivity issue, tedious washing steps, and cost efforts are the significant limitations. Kolosova et al. studied direct competitive ELISA for the AFB_1 analysis of food contents. They found the determinable range from 0.1 to 10 µg/L with an IC_{50} value of 0.62 µg/L (Kolosova 2006).

From the last decade, progressive exploration has been achieved in the construction of biosensor using several desired nanomaterials to improve the overall performance of the device. To overcome certain previously existing limitations, next to construct Label-free, simple, miniaturized, portable, and on-site monitoring of agricultural and food products using biosensors. Therefore, in the context below, we have summarized the work done in the areas of electrochemical biosensors such as voltammetric, impedimetric, potentiometric sensor, and optical biosensors such as surface plasmon resonance, fluorescence for AFB_1 detection where special emphasis is focused on the published reports that used nanostructured materials as a transducer matrix to fabricate the biosensing device.

The biosensor as a tool for analysis of AFB_1

The development of biosensor has been grown rapidly in the past few years for quantification and analysis of target analyte because it provides a precise and accurate result, fast response in a short time. It is an analytical tool that measures the biochemical response by generating recognition signals proportional to the target analyte concentration. It is a useful and sensible diagnostic device for clinical as well as non-clinical monitoring purposes such as food analysis, environmental field monitoring, medical diagnostic like glucose assay, laboratory examination, etc.

In general, the biosensor is composed of three major parts, as shown in Fig. 4, namely immobilization matrix (nanomaterials, conducting polymer), biological recognition element (tissue, microorganisms, protein, cells, an antibody, aptamer) and transducer (electrical, optical, mass and thermal). This review is focused on the fabrication and performance of various nanomaterials integrated biosensors for AFB_1 detection.

With the development of nanomaterials and biotechnology, electrochemical and optical biosensors integrated with nanomaterial have been widely employed in diagnostic devices. The order of improvements have come under consideration by using the anisotropic nanomaterials for electrode fabrication results to improve the characterstic parameters of the diagnostic device such as sensitivity, specificity, reproducibility, limit of detection and wide detection range (Li et al. 2020). When compared with traditional techniques, advances achieved in nanomaterials based biosensor are highly commendable. The use of nanomaterials on the electrode surface provide conducive functional groups, improve surface-to-volume ratio,

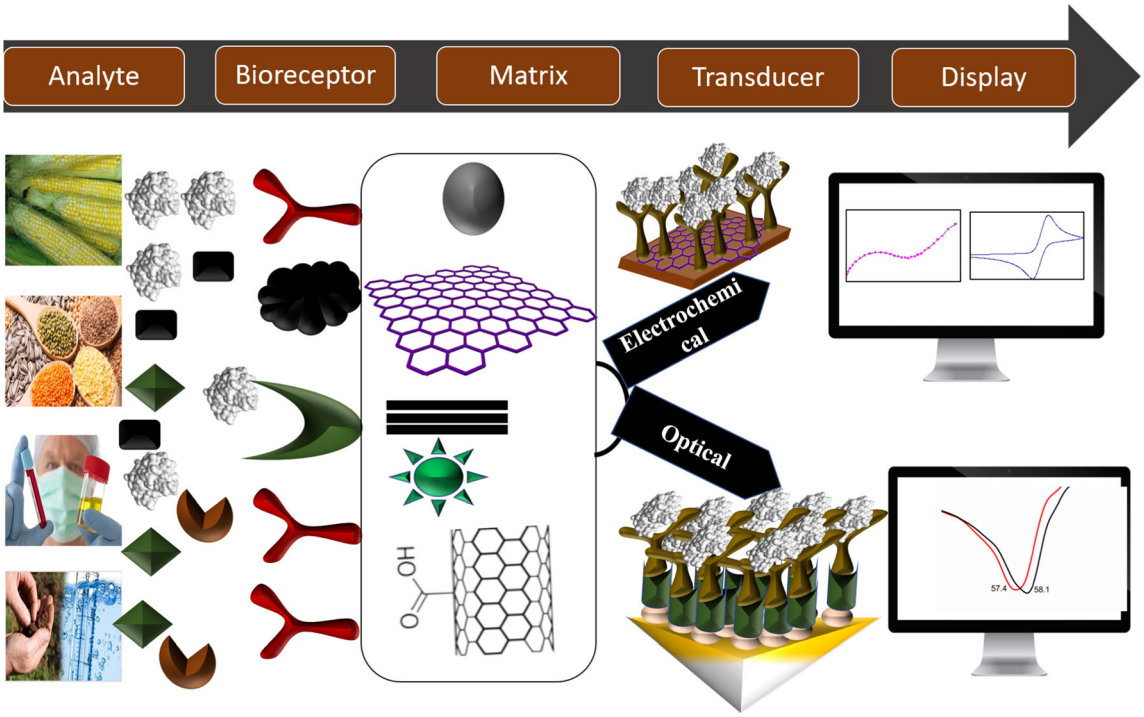

Fig. 4 Important components of the biosensor

enhance electrical or optical performance due to the physiochemical characterstics, improve electron transportation path between electrode surface and redox probe. Real-time diagnostic monitoring, miniaturization, wide range of detection, rapid detection time are the important characterstics of the fabricated biosensor which can be directly used for testing of agricultural food samples. Currently, researchers are mainly focused on the implimentation of optimal performance as detect low concentration, more stability and durability of the sensor for small molecule analyte using the nanomaterials in their construction. The major advantages of nanobiosensor over the conventional methods are user-friendly, rapid, cost-effective quantitative method for real-time monitoring of mycotoxins, promising diagnostic tool, high sensitivity, highly specific, portable, used for multiple mycotoxins detection on a single device, suitable for screening (Rai et al. 2015). Apart from the existence of several advantages in nanobiosensor technique, certain limitations or challenges are also remains which need to be overcome to develop the commercialized product for the food toxin analysis. Major issue is to use the suitable and sustainable nanomaterial which enhance the stability of the immobilizing matrix and durability of the device. Another major concern is regarding the disposable of devices and materials after ensuring the toxicity of the mycotoxins (Rai et al. 2015). Therefore, many researchers are mainly focused to improve efficiency of the analytical device and safe disposal after use. Hence, in this review article, brief description about the background of food toxin, outbreaks, available conventional techniques and their limitations, latest trends to detect food toxin in food samples and fabrication of devices have been described.

Table 1 describes the summarization of work reported on nanomaterials integrated electrochemical and optical biosensor for AFB_1 detection.

Role of nanomaterials

From the last two decades, nanobiotechnology and nanomaterial science play a significant role in the development of novel sensors and biosensors, mainly in the food industry, agricultural industry, and clinical laboratories (Durán and Marcato 2013). Nanomaterials are low dimensional materials comprising building units of submicron or nanoscale size at least in one direction (Durán and Marcato 2013). These materials can be nanotubes, nanoparticles (NPs), nanosheets, composites, and their structure functionalization, modification, further lead to improve several intriguing properties (Shipway et al. 2000). The key attractive feature to utilize dimensional nanomaterial mainly to provide the desirable conjugation to biomolecules, interesting optical and electrical properties such as narrow emission, broad absorption, large surface-to-volume ratio, high electrical conductivity, biocatalytic activity and many more that improve the

Table 1 List of some nanomaterials integrated electrochemical and optical biosensor for AFB_1 detection

S. no.	Type of detection method		Type of nanomaterial		Detection limit	Detection range	Time (s)	References
1	Eletro-chemical	DPV[16]	1-D[12]	SWCNTs/CS	0.0035 ng^{-1} mL	0.01–100 ng^{-1} mL	–	Zhang, et al. (2016)
2		CV[17]	1-D	MWCNTs	0.08 ng^{-1} mL	0.25–1.375 ng^{-1} mL	15	Singh, et al. (2013)
3		CV	0-D[13]	PEDOT[1]/AuNPs/ ITO	0.0045 ng^{-1} mL	1–25 ng^{-1} mL	-	Sharma et al. (2017)
4		DPV	0-D/1-D	CNTs/PDDA[2]/ PdAu	0.03 ng^{-1} mL	0.05–25 ng^{-1} mL	-	Zhang et al. (2015)
5		CV	0-D	CS[3]-AuNPs/Au	0.12 ng^{-1} mL	0.2–2.0 ng^{-1} mL	720	Ma et al. (2016a, b)
6		CV	2-D[14]	r-GO[4]/ITO	0.12 ng^{-1} mL	0.125–1.5 ng^{-1} mL	-	Srivastava et al. (2013)
7		EIS[10]	0-D	ZnS[5]/APTES[6]/ITO	0.02 ng^{-1} mL	0.25–2.0 ng^{-1} mL	-	Bhardwaj et al. (2016)
8		EIS	0-D	GQDs[7]/ITO	0.003 ng^{-1} mL	0.1–2.0 ng^{-1} mL	-	Bhardwajet al. (2018)
9		Potentiometric	0-D	AuNPs/GCE[8]	87 ng^{-1} kg	0.1–5.0 μg^{-1} kg	2700	Li et al. (2016a, b)
10	Optical	SPR[11]		Au chip	2.5 ppb	16–200 ppb	350	Moon et al. (2018)
11		SPR		SAM[9] aminothiol	1 μg^{-1} mL	-	-	Park et al. (2014)
12		SPR	0-D	AuNPs beta cyclodextrin	1 pg^{-1} ml	0.001–23.6 ng^{-1} mL	-	Majzik et al. (2015)
13		Fluorescence	0-D	QDs-Rhodamine123	2×10^{-11} M	0.1–0.6 $\mu molmL^{-1}$	-	Zekavati et al. (2013)
14		Fluorescence	0-D	QDs-AuNPs	3.4 nM	10-400 nM	< 3600	Sabet et al. (2016)
15		Fluorescence	0-D	Polymer dots-[15]AgNPs	0.3 pg/mL	5 pg/mL-1 ng/mL	60	Nasirian et al. (2017)
16		Fluorescence	2-D/0-D	GO-aptamers-QDs	1 nM	3.2 nM-320 μM	-	Lu et al. (2015)

[1]poly(3,4-éthylènedioxythiophène)
[2]Polydiallyldimethylammonium chloride
[3]chitosan
[4]reduced graphene oxide
[5]Zinc sulphide
[6](3-Aminopropyl)triethoxysilane
[7]Graphene quantum dots
[8]Glassy carbon electrode
[9]Self-assembled monolayer
[10]Electrochemical impedance spectroscopy
[11]Surface plasmon resonance
[12]One-dimensional
[13]Zero-dimensional
[14]Two-diemnsional
[15]Silver nanoparticle
[16]Differential pulse voltammetry
[17]Cyclic Voltammetry

overall performance of the bioanalytical device (Sozer and Kokini 2009). Recent advances in Zero-dimension (0-D), One-dimension (1-D), and Two-dimension (2-D) nanomaterials integrated biosensors for Aflatoxins detection based on electrochemical and optical transduction principles have been reviewed.

0-D nanomaterials

0-D materials have shown their interest in the applications of LEDs, solar cells, transistors, biosensors, and bioimaging because of the confinement of electrons dimensions, where the size lies in the range of 1–100 nm. Various kinds of NPs such as metal NPs (Au, Pt, Pd, Ag), metal oxide NPs (Zinc oxide, iron oxide, tin oxide), semiconducting nanocrystals quantum dots (Zinc sulfide, cadmium disulfide, cadmium diselenide, graphene quantum dots (GQDs), Molybdenum disulfide, molybdenum diselenide, etc.), core–shell quantum dots, hollow spheres, carbon nano-onions synthesized, used for the electrochemical and optical biosensing application due to their remarkable properties such as biocompatibility, high surface-to-volume ratio, low toxicity, wide absorption, narrow emission band spectra, photostability, low reactivity, dispersibility, excellent electronic charge transfer properties. It has recently been reported that QDs can be used as a secondary or subsidiary agent to modify the primary electrode of a biosensor. Various research groups utilized metal NPs and semiconductor nanocrystal-based sensing platforms by adopting their novel synthesis process and tried to conjugate with another dimensional nanomaterial, which facilitates the biosensing performance. They can be used as label-free or labeled conjugated biomolecules to detect the target analyte. The deposition on the electrode matrix can be achieved by self-assembly, electrophoretic deposition, drop-casting, etc. to obtain a stable and functionalize film.

0-D Electrochemical Biosensor The electrochemical biosensor has widely been explored for the point-of-care diagnostic device, monitoring in clinical and non-clinical laboratories, as well as in industries, i.e., environmental or food control process. Intriguingly, electrochemical transduction between biorecognition element and analyte occurred at the electrode surface measured as an electrical signal in terms of potential, current, or impedance.

Voltammetric electrochemical biosensor: Voltammetric electrochemical technique refers to the measurement of the current signal produced by scanning the DC potential in three-electrode systems, where nanomaterials fabricated surface act as a working electrode, platinum act as a counter electrode and silver-silver chloride as a reference electrode.

Zero dimensional nanomaterials have been progressively utilized for the construction of electrochemical biosensors. Significant alteration occurs in the energy band gap by altering the size, shape, thickness, and fraction of sp^2 domain behavior lead to a change in the optical and electronic properties of the material.

The 0-D integrated electrochemical biosensor has been fabricated for the quantification of AFB_1 in food. The electrochemical system has been developed by Ma et al. using a one-step electro-deposition process for the fabrication of embedded electrochemical gold microelectrode (Ma et al. 2016a, b). A composite of Chitosan (CS) and AuNPs film offered functional amino groups for immobilization of antibodies on the sensor surface and electrochemical properties also increased due to the high electrical conductivity of the composite. Analytical performance was conducted using Differential Pulse Voltammetry (DPV) technique and 12 min was the sensor response time. Analytical current signal varied in the two linear detection ranges as function of AFB_1 concentrations from 0.1 to 1.0 ng/mL and from 1 to 30 ng/mL respectively with the limit of detection (LOD) of 0.06 ng/mL. The electrochemical system has been validated with spiked maize samples of AFB_1 with LOD of 0.19 ng/mL.

Another biosensor has been developed by the same authors Ma et al. for AFB_1 detection using advanced disposable and economic microelectromechanical system (MEMS) technology (Ma et al. 2016a, b). MEMS device is an attractive key technique in the food and healthcare sector mainly developed by microfabrication technique, which contains a mechanical and electro-mechanical element that able to display response in a short duration of time, little power consumption, deliver high performance and inexpensive sensor. Authors have been constructed the microelectrode disk-ring on the printed circuit board by photolithography process in a disk area of $1mm^2$ for the working electrode and ring area act as the counter electrode. On the working electrode, dispersed solution of CS and gold precursor was deposited using chronoamperometry technique at a constant potential − 1.1 V for 300 s. Abundant AuNPs uniformly distributed over the microelectrode surface which confirmed by AFM technique. This sensor worked in the ranges of 0.2–2 and 2–30 ng/mL with a low detection limit of 0.12 ng/mL with a sensitivity of 72.34 $\mu g\ ng^{-1}\ mL\ cm^{-2}$. The sensor responds within 24 s. Validation of the sensor has been done by spiked wheat samples and average recovery lies in the range of 90.4–105.7%.

An Electroless plated silver/cysteine biosensor platform has been developed by Wacoo et al. using the Cyclic Voltammetry detection technique (Wacoo et al. 2016). An Electroless deposition of silver onto glass slide has been performed followed by the immobilization of cysteine molecule for the covalent binding then antibodies of AFB_1 immobilized and blocking free cysteine groups using horseradish peroxide. Fabricated biosensor worked in the range of 0.06–1.1 ng/mL, with a limit of detection of 0.08 ng/mL. This sensor has shown précised performance

up to the 5 weeks and highly specific towards AFB_1 molecules.

Conducting polymers have also widely been explored in the fabrication of diagnostic applications such as biosensing and bio-imaging due to high conductivity and biocompatibility properties. Sharma et al. developed the AFB_1 biosensor using the conducting polymer of PEDOT (oxidative polymerized EDOT), which has been deposited onto the ITO electrode surface (Sharma et al. 2017). The positive charged polymer allowed the incorporation of negatively charged doping agents as AuNPs to balance overall charges, thereby led to improve electrical conductivity of the materials. The fabricated immunosensor exhibited amperometric sensitivity of 3.72 μA ng^{-1} mL in the linear range of detection of 1–25 ng/mL with a LOD of 0.0045 ng/mL. The real sample analysis has been performed in maize spiked AFB_1 concentrations of 30 ng/mL and 50 ng/mL and reproducibility found to be 96.13% and 94.5% respectively.

Graphene structural properties provide benign and facile environments in the fabrication of biosensing devices because they have unique electrical, mechanical, and optical properties such as high electrical conductive features, ease of functional groups, the high electron transfer rate between an electrode and electrolyte redox probe. Recently, a facile combination of GQDs-AuNPs has also been gained great interest to construct a sensor for analyte detection because it improved the bio-sensing characteristics. Recently, Bhardwaj et al. demonstrated the usage of GQDs-AuNPs composites to quantify AFB_1 in food content. Composite of GQDS-AuNPs has been chemically linked by using the 2-aminophenol as a crosslinker to conjugate COOH groups of GQDs to the NH_2 group of crosslinker via conjugation of a thiol group to Au NPs (Bhardwaj et al. 2019). Further, the composite has been transferred on ITO coated glass substrate by the electrophoretic deposition technique. This sensor worked in the range of 0.1–3.0 ng/mL by the addition of the analyte concentration of AFB_1 and low LOD of 0.08 ng/mL. Further, this fabricated biosensor has been tested with the real spiked sample analysis in maize. The electrochemical current signal dependently increased with increasing the AFB_1 concentrations in the range of 0.1–2.5 ng/mL and the regression coefficient found to be 0.99.

Impedimetric electrochemical biosensor: Electrochemical impedance spectroscopy is another common useful technique for analysing material properties and biosensing performances of the devices. In the three-electrode system, a small amplitude sinusoidal alternative current excitation signal applied which lies in the range of 2–10 mV in an applied frequency range (0.01–100 kHz) correspondingly impedance spectrum displayed in the form of the Nyquist plot (real and imaginary impedance). It is label-free detection techniques which able to provide information regarding the interaction of biomolecules with electrode surface, characteristics of the interfacial layer formation, charge transfer resistance response at electrode–electrolyte interface surface and so on.

Bhardwaj et al., developed electrochemical immunosensor for the AFB_1 detection using self-assembly of zinc sulfide quantum dots (Bhardwaj et al. 2016). In this assay, indium tin oxide (ITO) was hydrolyzed and treated with (3-aminopropyl) triethoxysilane (APTES) for the amine silanization process. Silanized electrodes treated with zinc sulfide quantum dots and antibodies of AFB_1 have been immobilized over the self-assembled electrode surface using EDC-NHS protocol (Fig. 5). Impedimetric immunosensor respond in the range of 0.25–2.0 ng/mL with a detection limit of 0.02 ng/mL. According to our insight, this fabricated AFB_1 biosensor showed high sensitivity and stability only with standard AFB_1 concentration, but authors did not perform the experiments with food samples which could demonstrate the realistic performance of the fabricated biosensor.

Another biosensor for food toxin detection has been developed by Bhardwaj et al., using graphene quantum dots (Bhardwaj et al. 2018). It has been reported that graphene has a zero-band gap and a low abundance of functional groups on their basal planes and edge planes resist their applications in various fields. Therefore, reducing the size of nanosheets improved hydrophobic edges and hydrophilic planes that have carboxylic and hydroxyl functional groups on the surface thereby enhance the electron transfer kinetics. Graphene quantum dots are one of the most promising desirable materials due to biocompatibility, non-toxic, optical, and electronic properties. The impedimetric biosensor for AFB_1 detection has been fabricated using Graphene quantum dots and the sensor was found to detect AFB_1 in the concentration range of 0.1–2.0 ng/mL with LOD of 0.003 ng/mL and sensitivity of 213.88 Ω/(ng/mL)/cm^2. The sensor has also been validated with real samples.

Also, the three-dimensional shape structured of nanoelectrode ensembles has been shown widely interest in the construction of biosensor due to their special configuration and large surface area. Hu et al. have developed poly(o-phenylenediamine) (PoDD) electropolymerized film modified gold three-dimensional nanoelectrode ensembles, fabricated by template synthesis in track-etched polycarbonate membrane (Hu et al. 2015). Label-free PoDD modified AFB_1 impedimetric electrode has shown good performance in immunosensing applications because of large active surface area, conductive nature and presence of conducive amino and imino functional groups. To specifically maintain the orientation of the antibody of AFB_1 to the electrode surface, staphylococcal protein A has been

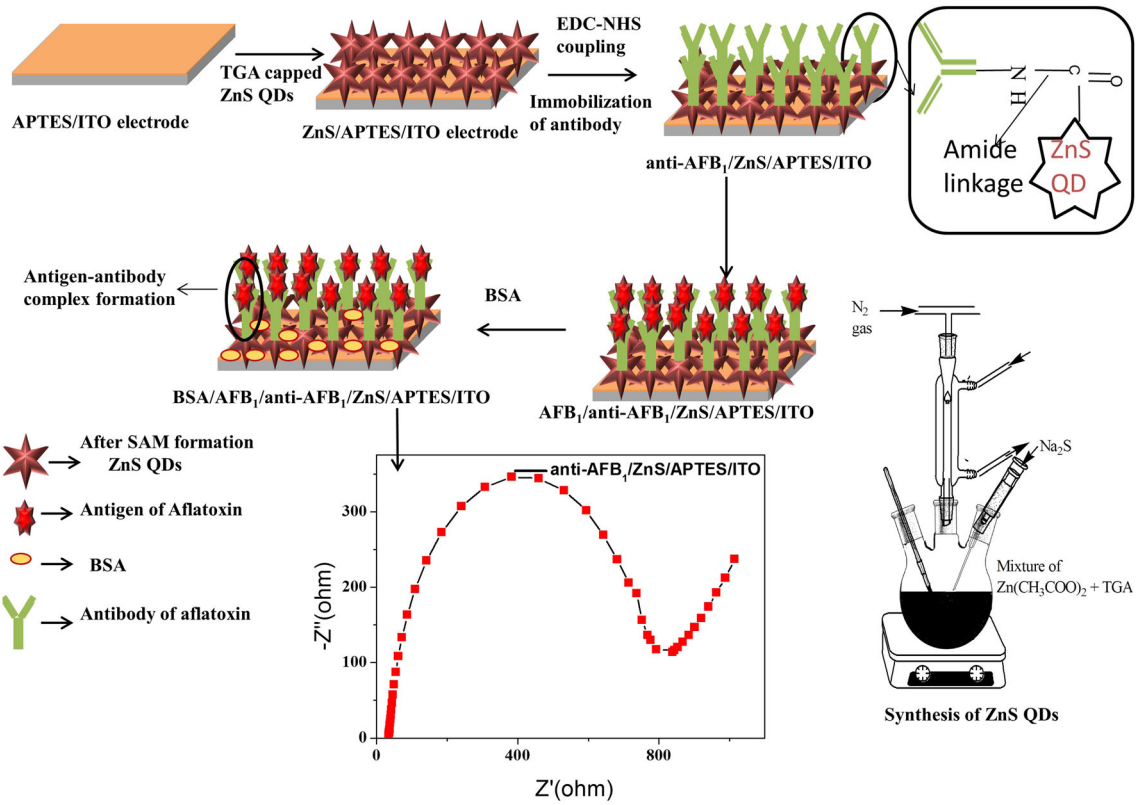

Fig. 5 Diagrammatic presentation of Zinc sulfide quantum dots based electrochemical immunosensor for AFB_1 detection (Bhardwaj et al. 2016)

used to directionally conjugation with AFB_1. The sensor showed linear changes in charge transfer resistance by increasing the concentrations of AFB_1 in the range of 3–100 ng/mL and LOD of 1.5 ng/mL. Spiked corn samples have also been tested using the fabricated sensor, and recovery of the samples found to be in the range of 89.2 to 105.8%.

Potentiometric electrochemical biosensor: The potentiometric electrochemical biosensor also utilized to investigate the antigen–antibody interaction using an ion-conductive membrane, which converts the biorecognition process into a response signal as electric potential. It measured the potential difference between the working electrode and the reference electrode under zero current ion fluxes.

Stepurska et al. have developed a potentiometric pH-sensitive field-effect transistor biosensor using acetylcholinesterase enzyme for AFB_1 detection in real samples such as peanut, walnut, and sesame (Stepurska et al. 2015). The dynamic range for AFB_1 detection from 0.2 to 40 µg/mL. However, the enzyme-based biosensor exhibits less sensitivity in the microgram detection range and unable to provide information about the presence of such low concentration of the analyte. In this context, many research studies have been conducted to improve the detection range in the nanomolar region of the biosensor.

Li et al. developed a potentiometric electrochemical biosensor for AFB_1 detection using a nanocomposite of AuNPs labeled antibodies of AFB_1 (Li et al. 2016a, b). The nanocomposite has been prepared using 16 nm of gold colloidal solution immersed into an antibody of AFB_1 solution and kept overnight to generate electrostatic and hydrophobic interactions between antibody and gold solution by adjusting pH from 4–6 to 9–9.5 using Na_2CO_3 aqueous solution. This fabricated biosensor worked in the range of 0.05–10 ng/mL with a LOD of 11 pg/mL. The accuracy of the developed potentiometric sensor has been validated in naturally contaminated and spiked peanut samples. RSDs values have been found to be less than 12%; revealed sensor could utilize for quantitative analysis of AFB_1 in foodstuffs.

0-D optical biosensor Over the last 10 years, many efforts have been devoted to developing an optical biosensor for mycotoxin analysis using optical SPR phenomenon and fluorescence detection methods. These techniques have widely been used for environmental monitoring, food analysis, clinical analysis, and biotechnology industry.

Surface plasmon resonance optical biosensor: An optical biosensor as surface plasmon resonance (SPR) has been proven an advanced technique due to the existence of

potential advantages such as *in-situ*, label-free, and real-time monitoring molecular phenomenon. It recognizes the interaction of biological elements with target analyte through changes in the refractive index of the material over the metallic surface. The SPR is a rapid and reliable label-free sensitive detection technique gives qualitative along with quantitative information about the target samples and fabricated sensor chip can be further reused for many analytical cycles. The SPR technique provides rich information about the affinity, specificity, kinetics of biomolecular interactions as an association or dissociation phase (Szabo et al. 1995). The commercialized BIAcore instrument was first released in the 1990s for the biospecific interaction analysis (Liu et al. 2017). The specific interaction of analyte analyzed by the simple interaction of immobilizing one molecule binding pair on sensor chip surface and injection of a series of analyte concentrations across the sensor surface. The phenomenal concept behind this variation is that when plane-polarized light directly illuminated through a prism surface to dielectric interface of metal/solution over a range of incident angle under the total internal reflection phenomenon meanwhile evanescent wave generated and at a selected incident light angle generated evanescent wave resonates with surface plasmons produced by the presence of free electrons on metal film conducting surface and after that dip resonance angle get generated in the spectrum denoted as SPR angle because energy of incident light has been utilized by the surface plasmon (Singh and Mehta 2020, Lee et al. 2018). Through the influence of species or biomolecules on the metal conducting surface, SPR sensorgram generated by measuring the shift in the reflective index against the time.

Fabrication of the SPR assay depends mainly on the utilization of the detection method as well as the size of the target analyte. Direct detection of the target analyte is easy for the larger size of molecules, where no need for competitive or sandwich immunoassay while measuring the signal for small molecules in real-time monitoring, is quite difficult due to the low mass of the molecule. As AFB_1 is a small molecule having low molecular mass, the changes caused by binding to the sensor surface may be too low to show a significant change in the refractive index. Therefore, conjugation of biomolecules with some nanomaterials or with other biocompatible proteins is the possible way to enhance the signal response and should be identified in the measurable region. Bio-functionalized nanomaterials such as AuNPs, magnetic NPs, quantum dots, have been widely used for optical detection of AFB_1. But still, it remains a great challenge to amplify the SPR signal with improved sensitivity due to small molecules of AFB_1.

The limited capacity of immobilization of biomolecules over the sensor chip restricts to obtain high sensitivity by SPR based diagnostic tool. Therefore, sensor chip surface architecture can easily be tailored by thin-film surface modification with multivalent compounds such as dextran or poly-aminoacid or by the protein immobilization to use the three-dimensional space on the sensor surface. For example, Park et al. developed a rapid detection method for AFB_1 by a functional protein crosslinker using the SPR technique (Park et al. 2014). The gold electrode chip surface was modified by self-assembly of aminothiol, followed by the protein G crosslinker. The protein G has a strong affinity to bind with the antibody orientally. The change in SPR signal intensity observed in the range of 1–100 μg/mL and LOD of 1 μg/mL. Validation of the fabricated sensor has been tested in spiked corn samples by various AFB_1 concentrations from 0.5 to 15 μg/mL. The most significant change in the SPR signal has been observed with 15 μg/mL of AFB_1 concentration and no change in the SPR signal has been found with 0.5 μg/mL. The fabricated sensor found to detect up to 1 μg/mL concentration of AFB_1. Although this sensor shows in micro-level detection range and high detection limit for AFB_1, it is necessary to measure the AFB_1 in the nanomolar region which should be lower than the maximum permissible level by the European Union (2 μg/kg).

Recently, Moon et al. designed the SPR portable sensor for on-site detection of AFB_1 in grains (Moon et al. 2018). In this work, SPR Au chip treated with cysteine-protein G to orient directionally AFB_1 antibodies on the surface and the modified chip has been conjugated with AFB_1-BSA into the flowed system continuous to AFB_1 detection in the range of 16–200 ppb. Inversely proportional change in SPR response unit with AFB_1 concentrations showed the successful detection of AFB_1 with LOD of 2.5 ppb, and limit of quantification of 16.32 ppb. Further, validation of the fabricated SPR sensor has been done in spiked-rice, almond, and peanut samples (100 ppb AFB_1 concentration). A significant signal amplification has been observed with spiked samples revealed that the sensor can be utilized for on-site monitoring of mycotoxins.

Another term of Surface Plasmon Resonance is the Localized Surface Plasmon Resonance (LSPR), a powerful technique that works on the integration of metallic NPs over the sensor chip or conjugation of antibodies with metal NP. Nanoparticle-based optical sensors are widely useful for the quantitative detection of biomolecules such as an antigen, nucleic acid, uric acid, glucose detection. LSPR based detection technique mainly depends upon the size, shape, interparticle spacing as well as on the dielectric properties of the localized environment around the NPs because of the rapid decay of plasmon electromagnetic fields due to the increment in the separation between the metallic surface and the target analyte. The thickness of the biorecognition interface directly affects the sensitivity of

the optical sensor. The presence of NPs may probably increase surface-to-volume ratio which can easily conjugate with a significant amount of biomolecules therefore sensor shows improve sensitivity, stability, and the detection limit. Hu et al. designed the SPR sensor using the AuNPs to enhance the SPR chip sensitivity for AFB_1 detection (Hu et al. 2014). The SPR sensor chip rationale combined with the unique properties of poly(oligo-ethylene glycol) methacrylate-co-glycidyl methacrylate and LOD of 8 pg/mL.

Majzik et al. demonstrated the sensitive detection method for AFB_1 molecules onto the gold SPR disk using the functionalized AuNPs (Majzik et al. 2015). The thiol-modified cyclodextrin and gold β-cyclodextrin functionalized AuNPs immobilized onto the surface through covalent bonding. The response unit of the designed sensor quantitatively determined in the range of 0.001–23.6 ng/mL and LOD of 1 pg/mL without using any other analytical reagents.

Recently, a researcher in the field of science and technology have focused their contribution towards the Surface plasmon resonance imaging (SPRi) based multiplexing system to develop simultaneous detection of all mycotoxin on single sensor chip surface which saves both time and cost of the biological reagents. Also, able to respond to multiple sensing information of mycotoxins using the single injection of the analytes. Moreover, the demand for miniaturization of the Lab-on-chip based system has been explored in the last few years. Recently, the double-3-plex benchmark assay developed using SPRi flat gold biosensor chip by Joshi et al. for multiple analytes of mycotoxins detection in barley. Transferability of the state-of-art of the double-3-plex system into 6-plex SPRi portable assay using single nanostructured gold biosensor chip (Joshi et al. 2016) and the LOD of 0.6 μgKg^{-1} for AFB_1. The fabricated chip can be used for at least 60 cycles to measure the response signal.

Another multianalyte system has been developed by Wei et al., using the transduction SPR detection method. SPR sensor chip has been prepared by self-assembled polyethylene glycol solution and kept for a minimum of 12 days at room temperature in the dark for smooth and uniform assembly of layer on Au chip (Wei et al. 2019). Different mycotoxins antigen of AFB_1, Ochratoxin A, Zearalenone, and Deoxynivaleno have been spotted over the assembled single-chip and tested with antibodies. As a result, decrease in reflectivity response signal has been observed with different concentrations of AFB_1 from 0 to 128 ng/mL due to immunocomplex formation and LOD of 0.59 ng/mL. Although, the sensor has showed a multianalyte mycotoxins detection system on single-chip but required lengthy sensor chip preparation and incubation time in a solvent.

Label-free detection of small molecules using the SPR technique is a great challenge and also require substantial signal amplifier for the précised and accurate detection. Therefore, integration of nanoparticle like AuNPs remarkably increases the detection signal by generating plasmonic resonant coupling between NPs and chip surface (Fig. 6). Recently, Bhardwaj et al. demonstrated the comparative studies between related to the fabrication of self-assembled monolayer (SAM) and the influence of AuNPs on Au chip for AFB_1 detection using SPRi technique (Bhardwaj et al. 2020b, c, a). Fabricated functionalized AuNPs on Au chip surface and bare Au chip has been utilized for AFB_1 detection. Integrated AuNPs/Au chip has been responded in the range 0.01–50 nM AFB_1 concentration with a limit of detection of 0.003 nM while bare Au chip shows a linear range of detection from 1 to 50 nM with a limit of detection of 0.19 nM. Hence, AuNPs modified Au chip proven to clearly a better tool for the detection purpose. Also, fabricated AuNPs chip has been validated by spiked wheat samples and average percentage recoveries found to be in the range of 90.1–93%. Another work is published by the same research group, related to the use of anisotropic shape of nanomaterials for the fabrication of electrical and optical biosensor for AFB_1 analyte detection (Bhardwaj et al. 2020b, c, a). Anisotropic shape of Au as gold nanobipyramids (AuNBPs) have been synthesized using the CTAB as a surfactant and growth reagent further capping agent were exchange from CTAB to lipoic acid (Fig. 7a). Pure and monodisperse of AuNBPs of 70 nm base length deposited onto APTES film surface then electrical as well as optical studies has been carried out for AFB_1 detection (Fig. 7b). SPR based AFB_1 detection have been found to linear in the range of 0.1–500 nM with a limit of detection of 0.4 nM while impedimteric sensor has shown linear response in the range of 0.1–25 nM with a limit of detection of 0.1 nM. Also practical utility of the sensor have been tested in spiked maize samples and 95–100% of recovery found.

Fluorescence optical biosensor: Fabrication of optical sensors based on fluorescence phenomenon has also been grown with a lot of advancement for a point-of-care diagnostic tool, environment monitoring, food analysis, and so on. There are two types of molecules basically used to construct the fluorescence sensing technique. One that exhibits natural fluorescence without the addition of fluorescent labels while others that do not occur fluorescence naturally but to make a course of action by different labels or probes can directly get an attached to the target analyte by covalent linkage through functional groups. The various parameters have been examined in fluorescence-based biosensors such as fluorescence anisotropy, rate of energy transfer, decay time, quantum yield, and quenching efficiency (Tan et al. 2016). Among the presence of various

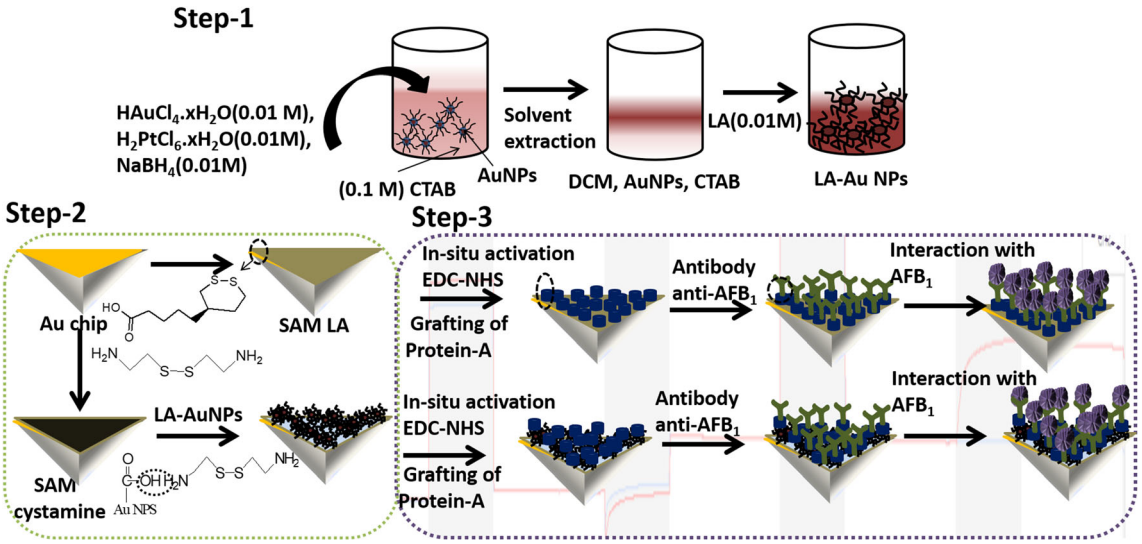

Fig. 6 Schematic illustrates the fabrication of optical biosensor for AFB_1 detection using bare Au chip and integrated AuNPs on Au chip surface (Bhardwaj et al. 2020b, c, a)

fluorescence sensor, aptamers based biosensor is widely accepted due to its high specificity and selectivity. Aptamers are short, artificially synthesized single-stranded oligonucleotide or peptide sequences transformed into the secondary or tertiary structure allow them to bind effectively to a specific target analyte with high affinity.

Recently, biosensor-based fluorescence detection has attained great interest using nano-labels or nanomaterials with carbon nanomaterials, NPs, quantum dots to improve sensitivity and selectivity for small molecules detection (Sharma et al. 2018). For example, Zekavati et al. developed a highly sensitive fluorescence resonance energy transfer (FRET)-based fluorescence immunoassay for AFB_1 detection using quantum dots as cadmium telluride (Zekavati et al. 2013). To recognize the target AFB_1 analyte, the FRET phenomenon occurred from AFB_1 antibodies, which have been immobilized on the shell of the quantum dot to rhodamine 123-labeled AFB_1 bound albumin. The feasibility of this developed method has been evaluated with various AFB_1 concentration in the range of 0.1–0.6 μmol mL^{-1} resulting in Rhodamine 123 fluorescence intensity dependently increased with increasing the concentration of AFB_1 and low LOD of 2×10^{-11} M.

In the past few years, organic labels or tags have been widely used to construct fluorescence sensors because of their ease of availability and quiet less expensive. Fluorescence dyes are common which made up of xanthene or cyanine but they have some drawbacks such as hydrophobicity and photo-bleaching properties are not the suitable factors for biosensing applications. However, recent progress has been achieved in the past few years, and efforts have been devoted towards the utilization of semiconductor or quantum dots based analyte detection. For example, the Fluorescence-based AFB_1 detection method developed by Lu et al., using the GO-aptamer-Quantum dot fluorescence quenching system (Lu et al. 2015). Cadmium telluride (CdTe) quantum dots have been synthesized and mixed with thiol modified AFB_1 aptamer further conjugated with 40 μg/mL concentration of GO via π–π stacking. In the presence of AFB_1, quantum dot attached aptamer interact with AFB_1 molecules and form folded AFB_1-aptamer complex. This assay exhibited good selectivity and showed a dynamic range of detection from 3.2 nM to 320 μM and LOD of 1.0 nM. Further, quantitative measurements have been carried in peanut oil samples. As a result, the fluorescence intensity increased by increasing the AFB_1 concentration from 1.6 nM to 160 μM and LOD of 1.4 nM. Using the simple fluorescence phenomenon that occurred from Donor to acceptor molecules, another biosensor has been developed by Sabet et al. (2016). CdTe quantum dots used as a donor and AuNPs used as an acceptor molecule for aptasensor of FRET-based AFB_1 detection. Due to the electrostatic interaction between exposed bases of aptamer and AuNPs, aptamer-conjugated quantum dots adsorbed on AuNPs led quenching phenomenon in the presence of AFB_1 concentrations ranging from 10 to 400 nM, respective fluorescence intensity increased and LOD of 3.4 nM. Moreover, validation of the fabricated assay has been performed with rice and peanut spiked AFB_1 concentrations in the range of 5–20 nM and recovery found of be 104.7–108% and 104.5–106% in rice and peanut samples, respectively. Also, the results have been compared with the HPLC technique.

Silver (Ag) nanomaterials as in the form of nanoparticles or nanoclustures are also utilized to fabricate the optical or electrochemical biosensor for mycotoxins

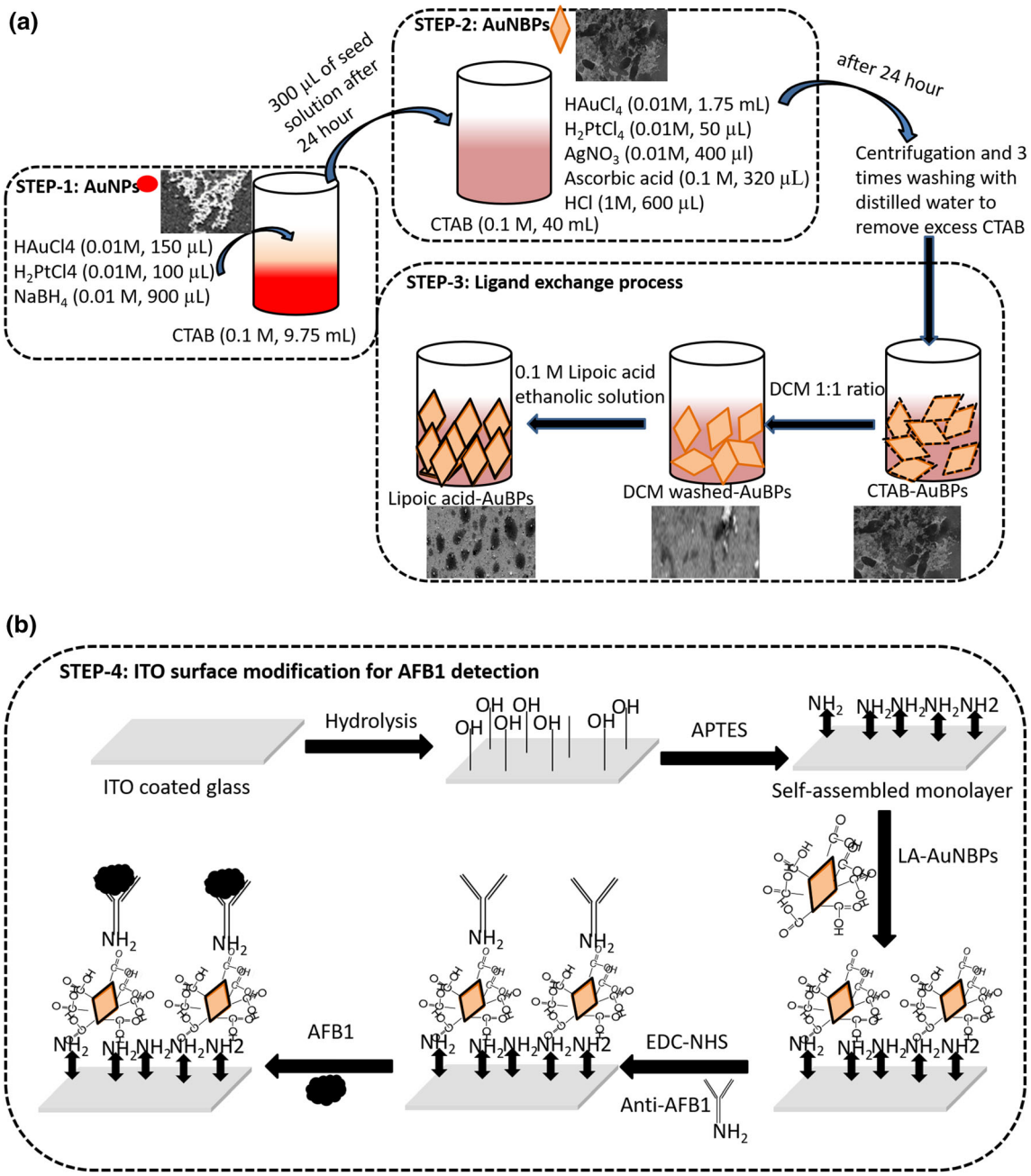

Fig. 7 Schematic depicts the fabrication of electrochemical and optical biosensor for food toxin detection using functionalized AuNBPs (Bhardwaj et al. 2020b, c, a)

detection. To fabricate the fluorosence biosensor, Ag can works in a dual functionality in the forms of FRET acceptor and supporting matrix onto the electrode surface. Therefore, integration of Ag nanomaterials in the fabrication of sensor device enahnce multiple-fold of rate constant in compared to bare fabricated device (Sharma et al. 2018). Furthermore, Ag NPs are also widely used to fabricate the biosensor for bioanalyte detect due to their excellent optical and electrical properties. Localised Surface Plasmon Resonance and Surface Plasmon Resonance bands of Ag effectively enhance absorption coefficient of the device. For example, Nasirian et al. developed ultrasensitive AFB_1 assay based on FRET from aptamer labelled fluorescence polymer dots to silver NPs labelled with complementary DNA (Nasirian et al. 2017). Using off–on signaling procedure in a FRET based nanobioprobe, AFB_1 concentrations have shown signal in the range of 5 pg/mL–1 ng/mL with a limit of detection of 0.3 pg/mL. The fabricated assay successfully validated in spiked wheat flour samples and found satisfactory agreement with ELISA. The use of Ag

nanomaterials to fabricate the biosensor for food toxin detection also improve detection range, limit of detection, sensitivity, reproducibility characterstics.

Magnetic NPs based immunoassay was developed by Xie et al. for AFB_1 detection using a porous graphitic-phase carbon nitride as a fluorescence probe and AFB_1-BSA conjugate modified with Fe_3O_4 as an immunosensing probe (Xie et al. 2018). Antibodies of AFB_1 were conjugated with porous graphitic carbon nitride nanosheets due to the presence of abundant active chemical sites using glutaraldehyde crosslinker. Magnetic NPs of Fe_3O_4 not only served as solid support but also facilitate the rapid separation and purification of immune-complex, which overall reduces the assay preparation time. Long-term one-month storage stability of fluorescence and immunosensing probe was attained at 4 °C. The rate of change of fluorescence was monitored at 355 nm emission with various AFB_1 concentrations. The fluorescence signal decreased by increasing the concentration of AFB_1 from 0.01 to 0.5 ng/mL and LOD of 0.002 ng/mL. Moreover, the applicability of the immunoassay was performed in uncontaminated maize samples, spiked-maize samples were analyzed with 0.05, 0.1, and 0.2 ng/mL concentrations. Percentage recoveries were found to be acceptable, which lies in the range of 98.0–135%, which indicates accurate fluorescence immunoassay for AFB_1 detection. In conclusion, the results of this fluorescence-based biosensor exhibit a quite limited range of AFB_1. Since the fluorescence and immunosensing probe stable up to one month at 4 °C could be suitable for the analysis food product.

1-D nanomaterials

The nanotube is used as building blocks for designing the biosensor that exhibits conductive and semi-conductive properties. Various nanotubes have been discovered and utilized for biosensing applications such as carbon nanotubes, zinc oxide nanotubes and titanium oxide nanotubes. Among them, carbon nanotubes paved great attention to constructing an electrochemical biosensor for AFB_1 detection due to low toxicity, fast electron transfer, high electrocatalytic activity, large surface area, and biological compatibility. Carbon nanotubes further classified as single-walled carbon nanotubes (SWCNTs) consist of single hollow spherical, containing 0.4–2 nm diameters, whereas multiwalled carbon nanotubes (MWCNTs) has a multi-hollow spherical cylinder formed by several concentric layers of rolled graphite whose diameter is 2–100 nm (Zhang et al. 2010). The variation in the diameter of SWCNTs tailors the electronic behavior of materials from conductive to semi-conductive properties. MWCNTs are considered as metals, whereas SWCNTs are considered as metal or semi-metal depending upon their construction configuration, i.e., armchair or zig-zag configuration. Those nanotubes having metallic properties are classified as in armchair configuration, whereas others who have semiconductor properties are of zigzag or chiral configuration. Electronic properties, catalytic properties, large surface area (1315 m^2/g) offer favorable conditions for immobilization of biomolecules through chemical bonding between the functional groups of carbon nanotubes and biomolecules results in the enhancement of electron transfer and optical signal which can be utilized for the detection of analyst by varying their concentrations. Uniform and well dispersed deposition of carbon nanotubes on the electrode matrix also play an important role in getting the conducive morphology for designing the high-performance biosensors for food toxin detection. Three methods have been used for their deposition, such as electrophoretic, drop-casting, or spraying to obtain the uniform coating of nanotubes where biomolecules should align adequately to the electrode to achieve the low leaching effect of biomolecules and provide smoothness resulting enhancement in the electro-catalytical signal.

1-D electrochemical biosensor Voltammetry electrochemical biosensor: Recently, Zhang et al. have developed electrochemical immunosensor for ultrasensitive detection of AFB_1 using SWCNTs and CS composite on the glassy carbon electrode (Zhang et al. 2016). To improve the dispersion ability and biocompatibility, linear polysaccharide CS was used. The electrochemical measurement has been conducted by DPV technique and quantitatively able to detect AFB_1 concentration in the range of 0.01–100 ng/mL with a detection limit of 3.5 pg/mL. In order to validate the feasibility of the fabricated sensor, naturally contaminated AFB_1 corn samples of concentrations 121.5, 40.5, 13.5 pg/mL assessed. Moreover, results have been compared with the HPLC technique, the relative error found in between − 4.4 and 8.4% revealed high accuracy of the sensor. In conclusion, SWCNTs shows advanced electrical characteristics with limited surface coverage area and electrical conductivity. However, the surface-to-volume ratio, bio-functionalization parameters get improved with the multi-layer of carbon nanotubes.

MWCNTs nanomaterials have also been utilized as a transducer matrix for the fabrication of biosensor. The highly sensitive and selective electrochemical immunosensor for AFB_1 detection have been developed by Chandan and co-workers in 2013 (Singh et al. 2013). Carboxylate MWCNTs have been chemically functionalized where carboxyl groups generated on the surface of CNTs and electrophoretic deposits on the ITO-coated glass electrode surface. The analytical performance of the designed immunosensor has been conducted by cyclic voltammetry (CV) technique in the detection range of

0.25–1.375 ng/mL, the detection limit of 0.08 ng/mL, and sensitivity of 95.2 μAng^{-1} $mLcm^{-2}$. This MWCNTs based immunosensor shows quiet limited concentration range of AFB_1, which could be improved by integrating some nanomaterials. The composite of nanomaterials as nanotubes with the polymer also facilitates the performance of biosensor, especially enhances the conductivity of the electrode, electron transfer rate, and provides stability.

Wang et al. developed an electrochemical imprinted sensor using o-phenylenediamine (OPD) as a monomer and AFB_1 as a template to synthesized molecularly imprinted polymer (MIP) membrane (Wang et al. 2014). Bimetallic NPs combination has been utilized as an alloy or core–shell structure that often exhibits improved catalytic properties than the monometallic particles. The exciting combination of Au/Pt bimetallic with CNTs, enhance the unique catalytic properties which directly impact on achieving an excellent heterogeneous electron transfer rate. The constructed immunosensor AFB_1/o-PDA/AuPt-MWCNTs/GCE exhibited excellent sensitivity and selectivity towards AFB_1 foodborne toxin. DPV response signal linearly decreased by increasing the AFB_1 concentrations from 1×10^{-1} mol/L to 1×10^{-5} mol/L with gradient constant incubated 4 min for each concentration and LOD of 3.0×10^{-11} mol/L. Spiked AFB_1 concentrations in rapeseed and hogwash oil have been used for the validation of immunosensor. Percentage recovery found to be 95.5–111.1%, and the relative standard deviation lies in the range of 2.30–4.70%.

However, aggregation tendency of CNTs through strong π–π stacking and van der Waals interaction results from the non-uniform and discontinuous film on electrode surface, but this factor could be reduced by integration into the positively charged polyelectrolyte that improves dispersion ability of CNTs in aqueous solution. Zhang et al. have designed an electrochemical immunosensor using Pd-AuNPs supported on functionalized carbon nanotubes poly(diallyldimethylammoniumchloride) (PDDA-MWCNTs) nanocomposite for AFB_1 detection (Zhang et al. 2015). The synthesized composite showed good electron transfer behavior attained high sensitivity with a detection limit of 0.03 ng/mL as by varying the AFB_1 detection range from 0.05 to 25 ng/mL. Also, the feasibility of the developed sensor has been investigated in a rice sample with different AFB_1 concentrations. Moreover, acceptable recoveries found to be 98.2–103.2%, and LOD of 1.25 μg/kg showed feasibility and applicability for another mycotoxin detection.

Impedimetric electrochemical biosensor: Costa et al., developed label-free electrochemical impedimetric immunosensor using self-assembly of a cysteine-modified gold electrode functionalized with CNTs (Costa et al. 2017). This sensor attained a low detection limit of 0.7 pg/mL in the range of detection from 0.1 to 20 pg/mL. The obtained high performance of label-free electrochemical biosensors could be facilitated to unified analysis, portable, and alternative monitoring tools for the analysis of crop storage.

The application of nanorods also utilized in the fabrication of biosensor, which enhances the quality, stability, compatibility with biomolecules as well as the surface area of the electrode. Bismuth oxide nanorods have been prepared by chemically and utilized for the development of immunosensor for AFB_1 detection (Solanki et al. 2016). Bismuth oxide nanorods provide large surface area, high diffusion coefficient, charge transfer rate constant, and enhance the electron transfer kinetics. The detection range of the developed sensor have been found to be 1–70 ng/dL with limit of the detection of 8.715 ng/dL, and the sensitivity of 1.132 $\mu A/(ng/dL)cm^{-2}$.

The miniaturization of the electrode in terms of portability, real-time detection, disposable is one of the promising approaches towards the rapid and inexpensive production of the biosensor. A disposable electrode based on the screen-printed with microelectrode leads the new possibility in the detection and quantification of the biomolecules. A label-free electrochemical immunosensor has been proposed for the sensitive detection of AFB_1 using the self-assembled gold nanoparticle onto the 1,6-hexandithiol gold electrode surface (Chen et al. 2014). The AuNPs not only enhance the electrical conductivity of the modified electrode but also offers the fast electron transfer efficacy, biocompatibility, and improved stability of the fabricated electrode. This proposed electrode showed a detection range of AFB_1 from 0.08 to 100 ng/mL, with LOD of 0.05 ng/mL.

Li and his groups, developed the portable electrochemical immunosensor for fast detection of AFB_1 in rice (Li et al. 2016a, b). The portable sensing element has been designed using the 3D printing USB compatible sensor. The screen-printed interdigitated microelectrode and portable detector achieved low cost, sensitive, and selective detection of AFB_1 in rice, and detection limit up to 5 ng/mL. The total detection time of the sensor is less than 1 h.

2-D nanomaterials

The 2-D structure of nanomaterials, i.e., nanosheets or layered materials whose thickness varies from 1 to 100 nm. The most exciting and widely used nanosheets are graphene nanosheets, made up of a single carbon atom packed with a 2-D hexagonal structure. Graphite is used as a transducer for the electrode fabrication to enhance the sensing signal along with the stability, reproducibility, and sensitivity of the sensor because of the large surface area (2630 m^2/g), electrical conductivity and remarkable

mechanical strength (Sadeghi 2016). The simplest and easiest way to synthesize graphene is chemical exfoliation and reduction of graphite or unzipping the carbon chain. Various functional groups have been generated on the surface of nanosheets through chemical exfoliation and functionalization of basal and edge planes. Addition of functional groups to GO, open not only the opportunities for variation of bandgap but also offers an option to tune electronic, optical, and catalytic properties. Several strategies have been developed to prevent the re-stacking of nanosheets and improve graphene dispersion in solvents. Further, electrochemical and electrocatalytic properties improved the interaction between biomolecules and electrode surface. The unique electronic structure of graphene exhibits delocalized π-bonds above and below the planes. This localized electron creates electrical conductivities and mobility of graphene within the planes. It has been widely studied that the incorporation of nanomaterials such as CS, NPs, and nanotubes to graphene sheets improves the important characteristics of the biosensor.

2-D electrochemical biosensor Voltammetry biosensor: The integration of a 2-D graphene sheets-based biosensor improves several intriguing properties owing to their unique physicochemical properties. For example, Srivastava et al. have constructed chemically reduced graphene oxide (rGO) modified ITO substrate to detect AFB_1 via antigen–antibody interaction (Srivastava et al. 2013). To synthesize the desired amount of active functional groups containing rGO sheets, 50 mM sodium borohydride used as a reducing agent while maintaining the pH of the solution at 10.0 by sodium carbonate. The electrophoretic deposition process utilized to place rGO on the ITO substrate matrix. CV measurements have been carried out with various AFB_1 concentrations ranging from 0.125 to 1.5 ng/mL with LOD of 0.12 ng/mL and sensitivity of 68 μA ng^{-1} mL cm^{-2}.

Indeed, decoration of NPs on graphene architecture potentially provides effective systems desire to amplify sensing signals. Another electrochemical biosensor developed by the Srivastava and their co-workers, for AFB_1 detection using the composite of 2-D–0-D nanomaterial of gold@rGO. The sensitive label-free electrochemical immunosensor has been designed by decorating AuNPs over the rGO sheets using the *in-situ* growth process where gold chloride trihydrate used as a precursor (Srivastava et al. 2015). The novel composite of gold@rGO improved the electrocatalytic activity, enhanced heterogeneous electron transfer rate, as well as the surface-to-volume ratio over the glass electrode. The developed CV-based AFB_1 immunosensor showed high sensitivity and specificity in the concentration range of 0.1–12 ng/mL with a low LOD of 0.1 ng/mL. However, lack of information about the practical applicability of the fabricated immunosensor for real sample analysis is a major limitation to validate the performance of the sensor.

Recently, Althagafi et al. developed an electrochemical biosensor for AFB_1 detection using a layer-by-layer deposition method to depose rGO-Au nanostructure over the ITO substrate (Althagafi et al. 2019). Thin layer rGO deposed by applying the negative potential − 0.16 V for 10 s to a solution of 4 mg/mL of GO in 0.1 M of sodium sulphate as an electrolyte followed by decoration of Au nanostructure over the rGO/ITO substrate by applying 0.9 V for 30 s. The smooth film formation enhances surface-to-volume ratio, electrical conductivity, and Raman Effect. The biosensing performance of the sensor has been determined by the CV and Raman technique. This sensor worked in the range of 100 ng/mL to 1 pg/mL of AFB_1 concentrations and LOD of 6.9 pg/mL. Moreover, validation of the fabricated sensor has done in spiked peanut samples using the concentrations of 10, 50, and 100 ng/mL, and average percentage recoveries found to be in the range of 97.6–102.8%.

Impedimetric biosensor: 2-D nanomaterials fabricated electrochemical impedimetric sensor developed by Srivastava et al. using the graphene oxide surface matrix for the detection of AFB_1 (Srivastava et al. 2014). Biosensing electrochemical response of the fabricated immunoelectrode has been found in the detection range from 0.5 to 5 ng/mL with a detection limit of 0.23 ng/mL and sensitivity of 639 Ω ng^{-1} mL cm^{-2}. Stability studies have been performed revealed that immunoelectrode stable up to 5 weeks. However, the graphene oxide material synthesis process is quite long, time-consuming, and has low electrical conductivity which restricts potential application biosensor. So, facile combination with other conductive material can help to improve the electrical conductivity and bioanalytical performance of the device.

The combination of graphene with polymer also provides spectacular improvements in mechanical and electrical properties due to strong interfacial adhesion between the graphene and polymer that generated through covalent or non-covalent interaction such as electrostatic, Van der Waals, π–π stacking. Recently, Linting et al. have proposed an ultrasensitive detection method for AFB_1 based on graphene/conducting polymer with an ionic liquid. Favorable microenvironment for the immobilization of antibody and improvement in an electron transfer rate increased the sensitivity of the sensor (Linting et al. 2012). Using impedance spectroscopic technique, biosensor showed the dynamic range of detection from 3.2 fm to 0.32 pm, and a detection limit of 1 fm with the long-term stability of the immunosensor up to 26 weeks.

Among the extensively utilization of graphene based 2-D materials, transition metal dichalcogenides of

molybdenum disulfide (MoS_2) nanosheets have also widely been explored to fabricate the biosensor devices due to low charge transfer resistance value, high electrical conductivity, and large surface area. These superb electrical and chemical properties are well-suited for electrical bio-system. Structurally, MoS_2 nanosheets possess hexagonal crystallite ordered in a manner of S–Mo–S through van der Waals force of attractions where each sheet made up of three layers comprising a molybdenum atom between two layers of the sulphur atom (Bhardwaj et al. 2020b, c, a). These sheets exhibit significant intrinsic band gap and considerable charge carrier mobility in a single layer or few layers in comparison with other materials that have an insignificant band gap like graphene material. Therefore, improvement in vertical charge transportation is achieved by decorating the nanosheet with nanoparticle. Recently, Bhardwaj et al. published an article on the use of MoS_2@GQDs composite based impedimetric immunosensor for AFB_1 detection (Bhardwaj et al. 2020b, c, a). Schematic illustration of synthesis of composite of cetyltrimethyl ammonium bromide (CTAB)-MoS_2 nanosheets with GQDs, deposition on ITO coated glass electrode and fabrication of biosensor for AFB_1 detection is shown in Fig. 8. CTAB-functionalized MoS_2 nanosheets have been prepared by chemical exfoliation process further decorated with synthesized GQDs nanomaterial for easier vertical charge transportation, carrier mobility, better immobilization process and effective bio-nanoconjugation. Label-free impedimetric immunosensor have been fabricated, works in the range of 0.1–3.0 ng/mL with a limit of detection of 0.09 ng/mL. This sensor has been tested with spiked maize samples and good percentage of recovery has been found (80.2–98.3%).

Recent trends in paper-based and micro-spotted array microfluidic AFB_1 biosensor

Microfluidics analytical technology has extensively been explored in the past few years because of the integrated concise analyte analysis onto a single lab-on-chip device. For a biomedical diagnostic point of view, this technology exists several benefits in terms of ability to sense in the presence of a minute concentration of sample volume and detection analyte, requires less amount of reagent, less energy consumption, low fabrication cost, and miniaturized microfluidic device as well as their flexible design (Miklós et al. 2020). Microfluidic device exhibit a concept of micro total analysis system where whole setup function have been performed onto a single device in micrometer level embedded with microchannels ranging from 10 to 200 µm with controlling the tiny amount of fluids (Ashraf et al. 2011). Microfluidic devices based biosensor for AFB_1 detection has attained a significant advancement in the past decades that could achieve high sensitivity and low LOD along that it can detect the multianalyte on a single chip and portable for on-site monitoring.

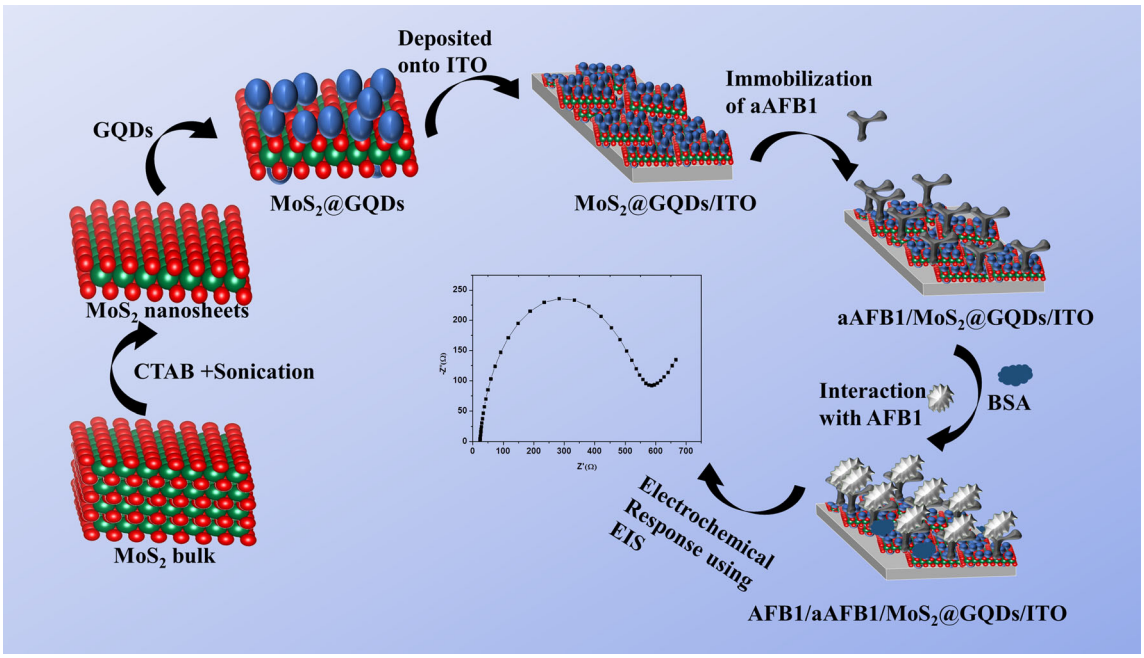

Fig. 8 Schematic illustration of synthesis of MoS_2@GQDs composite and fabrication of electrochemical biosensor for myctoxin detection (Bhardwaj et al. 2020b, c, a)

New immunoassay system has been established based on microfluidic paper-based analytical device (μPADs) fabricated through photolithography for small size analyte detection by colorimetric method. Two different paper substrates of Whatman filter paper grade 41 and Ahlstrom filter paper grade 319 have been used for paper sensor fabrication and three main channels have been designed, namely control and test zone, sample introduction zone, and a competitive capture zone (Busa et al. 2016). The simple competitive immunoassay developed by HRP-catalyzed 3,3′,5,5′-tetramethylbenzidine (TMB)-hydrogen peroxide (H_2O_2) assay for food testing in biotin and AFB_1. The bluish yellow-green product with different intensities revealed the presence of different concentrations of AFB_1 after the incubation from 6 to 9 min. The LOD of this immunoassay of 1.31 ng/mL. As per our insight, authors developed simple competitive ELISA microfluidic paper-based devices with quiet limited range of detection and tedious time required for the fabrication of μPADs device are certain demerits of the sensor.

Modal et al. have utilized decorated Pt NPs over the carbon nanofibers for AFB_1 detection. Microfluidic straightforward method has been developed using the functional micron, submicron, and nano-channel in a porous carbon film (Mondal et al. 2016). Carbon microchannels were produced by carbonization of a composite of electrospun poly (methyl methacrylate) (PMMA) nanofibers embedded in polyacrylonitrile (PAN) film. Further, Pt NPs decorated over the carbon nanofibers used for the surface functionalization of antibodies of AFB_1, followed by AFB_1 detection in the range of 10^{-12} g/mL to 10^{-7} g/mL with LOD of 1 pg/mL. Moreover, comparison studies have been made with and without embedded microchannels on carbon electrode decorated PtNPs. Fast electron transfer and aligned nanochannel for antigen–antibody interaction improved electrochemical sensor performance.

Chen et al., have developed a simultaneous detection strategy of four mycotoxins, i.e. T2-toxin, AFB_1, ochratoxin A, Zearalenone based on microfluidic and protein three-layered microarray consisting of PMMA (3 mm), adhesive (0.1 mm) and glass layer (1.1 mm) (Chen et al. 2018). Microfluidic based AFB_1 sensor works in the range 0.12–7.19 ng/mL and detection limit of 0.03 ng/mL and limit of quantification of 0.12 ng/mL. Small size, user-friendly custom made microdevice able to detect simultaneously four mycotoxins in real corn samples with the response time of 30 min. Fabricated sensor has been tested in spiked AFB_1 concentration in corn samples (0–6 ng/mL) and percentage recoveries found to be in the range of 90.70–102.0%.

Abdallah et al., developed an electrochemical lab-on-chip sensor for AFB_1 detection based on the voltammetric transduction principle (Ben Abdallah et al. 2019). The screen printing technology used to construct a three-electrode microchip followed by the integration of PDMS for static analysis. On the gold working electrode, further functionalization steps have been performed for conjugation of antibodies and detection of AFB_1. The technique has several advantages as it has great potential for the fabrication of miniaturized and portable devices using a very small 1–2 μL volume for analysis. This immunosensor works in the range of 50 fg/mL–5 ng/mL and LOD of 50 fg/mL responds in 30 min waiting time. The applicability of this sensor has been performed in rice milk spiked (1–2.5 pg/mL) and average recoveries found to be 27%. However, prolonged incubation time taken strategy is one of the limitations for practical applications.

Another paper-based low cost and disposable electrochemical immunosensor have been developed by Migliorini et al. for AFB_1 detection (Migliorini et al. 2020). This electrochemical immunosensor first prepared by waterproof paper substrate and low cost graphite-based conductive ink through simple cut-printing method. Further, working electrode have been functionalized by MWCNTs/CS materials through a drop-casting method. Monoclonal antibodies of AFB_1 have been immobilized using EDC-NHS corsslinkers. Electrochemical biosensing signal of the fabricated immunosensor analyzed by electrochemical impedance spectroscopy technique and sensor works in the ranage of 1–30 ng/mL with a limit of detection of 0.62 ng/mL. Also, paper-based fabricated immunosensor have been tested in maize samples yielded recovery of 97–99%. These results demonstrated the possible use of paper-based detection of AFB_1 in food samples.

A microfluidic paper-based analytical device highly useful over the available traditional technique as ELISA due to low-cost of operation, sample instrumentation, and user-friendly (Kasoju et al. 2020). It can provide a tool for on-site monitoring of food toxins in a less than minute which is a key factor for quantitative and qualitative analysis in food safety. Kasoju et al. developed microfluidic paper based rapid and sensitive device for AFB_1 detection using specific aptamer as a biorecognition element based colorimetric assay (Kasoju et al. 2020). Colour based changed in AFB_1 concentration have been observed when analyte reacts with specific aptamer followed by salt induced aggregation of AuNPs as an indicator. This microfluidic based biosensing device respond in the range of 1 pM to 1 μM of AFB_1 concentration, with a limit of detection of 10 nM.

Conclusions and future prospects

In summary, this paper contained literature search on the foodborne toxin of AFB_1 mainly occurs in food and feed materials that show human carcinogenic chronic diseases

and maximum allowed permissible limits to consume contaminated food products by National and International organizations. Also, a brief discussion has been made on the available conventional methods over the advanced detection device as a biosensor. The recent progress in the opto-electrochemical biosensing systems for food toxin detection have been summarized in this review article and results demonstrate that the significant enhancement in biosensing parameters of the device using nanomaterials are highly useful for ultrasensitive detection of toxins in practical agricultural spiked/non-spiked samples. Effective utilization of 0-D nanomaterials to fabricate the biosensor, as well as the decoration of 0-D nanomaterials on the 2-D nanomaterials, improved the biosensing performance of the sensor due to large surface-to-volume ratio, good optical and electronic properties, helps to improve nano-bio conjugation and stability. Therefore, nanomaterials owing to their potential physiochemical properties can provide effective ways to design ultrasensitive biosensors. Recent developments in the areas of microfluidic devices with micro-spotted array integrated with anisotropic shape of nanomaterials have been discussed. Apart from the laboratory investigations, several technical challenges are still remain for the commercialization of the fabricated devices to dialy usage for a common man. Large scale sample preparations of biocompatible nanomaterials, multiple miniaturized electrodes fabrication and ultrasensitive biosensing signal generations can improved the industralization of the devices. Furthermore, fabrication of biosensing device integrated with microfluidic technique or microarrray increases the efficiency of the device, multiple analyte detection on single chip and enhance large-scale applications. Production of electrical and optical biosensor for commercial use, continous and real-time monitoring of mycotoxins in complex environment can be obtained by using the anisotropic morphology of nanomaterials which should enhance sensitivity, reproducibility, specificity and multiple-analyte biosensing system and will explore more advanced prospects in the design and development of ultrasensitive devices.

Availability of data and material

Available data and materials in this work are properly cited and data is transparent.

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Consent to participate Informed consent was obtained from all individual participants included in the review.

Consent for publication Presented work has not been published or under consideration in any other journal and copy right permission is taken to reprint individual's image.

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