



Monitoring of Microbial Safety of Foods Using Lectins: A Review

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Food-borne diseases are on the rise, and these will likely continue as a public health concern into the coming decades. Majority of foodborne outbreaks are linked to infections by emerging foodborne pathogens such as *Campylobacter*, *Salmonella*, *Listeria monocytogenes*, and *Escherichia coli* O157:H7. Foodborne pathogen identification becomes crucial in such scenarios to control these pathogens, associated outbreaks, and diseases. Pathogen detection systems have evolved as essential food safety tools to combat microbial threats and experts are striving to develop robust, accurate and ergonomic rapid pathogen-detection kits. Lectin, a ubiquitous biomolecule (sugar binding proteins) present in almost all domains of life is a promising alternative to molecular based methods as a bio-recognition molecule in detection of foodborne pathogens for biosensor applications, owing to its multivalency and spatial organization of ligands. Due to their extensive prevalence, lectin-based biosensors have become the most sought-after bio-recognition molecules in biosensor applications because of increased sensitivity and reduced cost when compared to immune-based biosensors. The current paper discusses the claimed benefits of lectin as a superior bio-recognition molecule, as well as its numerous applications in biosensor creation.

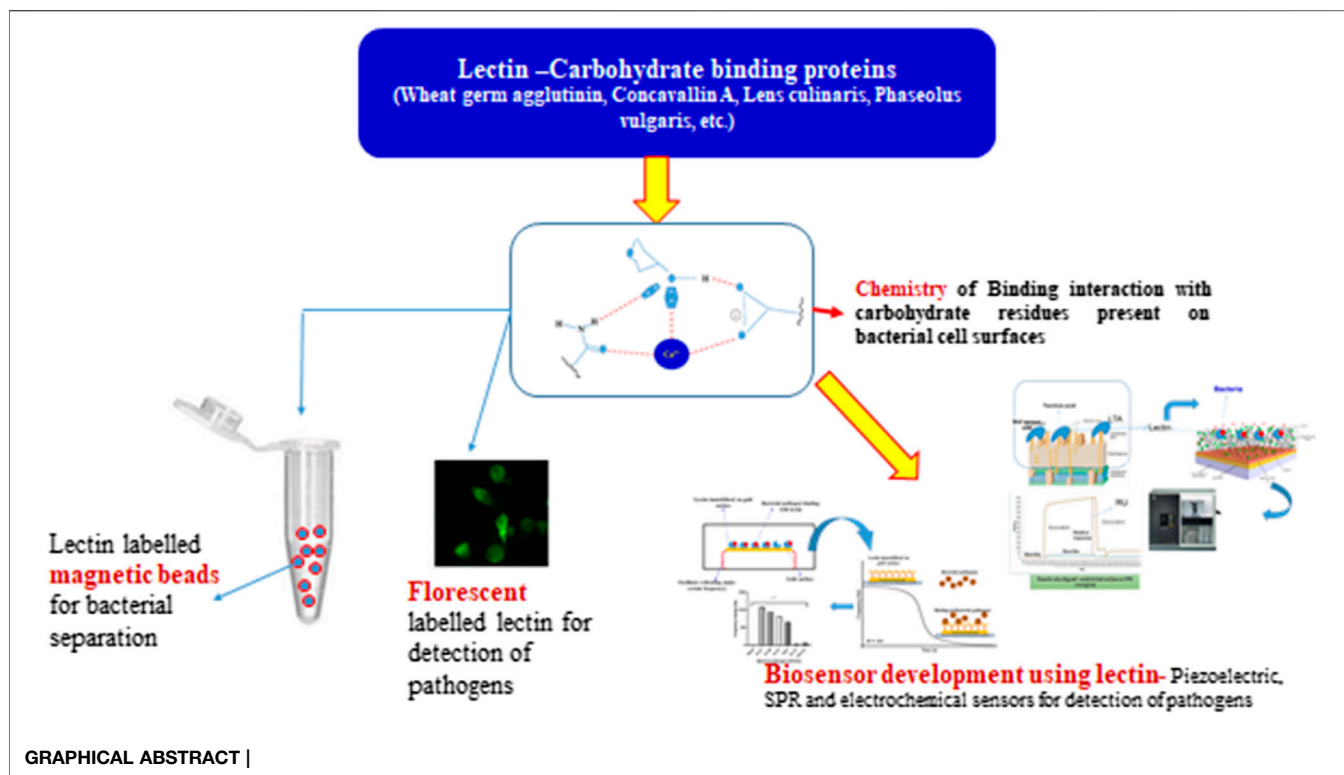
Keywords: food safety, biosensor, lectin, SPR, food borne pathogens

HIGHLIGHTS

- The food safety researchers are working hard to create rapid pathogen detection tests that are reliable, accurate, and easy to use.
- Lectin, a common biomolecule also known as sugar binding proteins, has been proven to be a promising bio-recognition molecule in the detection of foodborne infections.
- Lectins are the most sought-after bio-recognition molecules in biosensor applications due to their increased sensitivity and reduced cost.
- For the detection of food-borne diseases, lectins have been widely used in the fabrication of piezoelectric, optical, and electrochemical biosensors.

INTRODUCTION

Foodborne diseases have become a major global public health concern in the last three decades, with considerable increases in incidence (Ramirez-Hernandez et al., 2020). Consumption of tainted food



and water has resulted in 3-5 billion illnesses and almost 1.8 million deaths in young children per year, primarily owing to diarrheal disorders (WHO, 2015). About thirty-one identified food-borne diseases (mostly bacteria and viruses) have been reported in the United States alone (Sachdev et al., 2021). The bulk of disease outbreaks in impoverished nations go unreported and unrecognized as part of the health or financial losses sustained due to a lack of awareness and insufficient medical services. Controlling and managing outbreaks by effective tracing and recalling of contaminated goods become difficult in these circumstances, which exacerbates foodborne diseases. Moreover, developing strategies for identifying the causes linked to contamination, preventing future incidents, and reinforcing food safety rules and platforms is becoming a difficult issue (Vemula et al., 2012).

As a result, it is critical to diagnose food products, particularly ready-to-eat (RTE) foods, for contaminating microorganisms and other chemical contaminants in order to prevent these new foodborne infections and disorders. The farm-to-fork approach to food safety is becoming increasingly popular (Faour-Klingbeil, 2017). Old culture-based methods for detecting bacterial diseases still rely on traditional methods, needing a 5–7-day regimen for successful identification of the causal bacterium (Wu and Zeng, 2017). Though these approaches are recognized as gold standards because they are generally well established and validated, their length and poor speed make them ineffective and outdated in the face of food production and storage deadlines. Due to their increasing sensitivity and speed, genotypic approaches for detecting these pathogenic

bacteria have recently surpassed classic microbiological methods. Because of their great accuracy and sensitivity, molecular approaches based on polymerase chain reaction (PCR) and 16S rDNA/amplicon sequencing have surpassed time-consuming conventional procedures (Hameed et al., 2018). However, there is a catch: these approaches necessitate the use of complicated devices and expert employees.

In addition, using biosensors to identify microbiological and chemical pollutants in food is a unique technique and a possible alternative to traditional analytical approaches. In terms of sensitivity, specificity, selectivity, reliability, efficiency, and robustness, biosensors are quick and outstanding. Furthermore, biosensors allow for real-time monitoring of food pollutants and have revolutionized detection procedures, resulting in the creation of quick and specific detection tests that provide precise and immediate results. A biological component (a bio-recognition molecule that identifies and creates a signal), a signal transducer, and a reading device make up a biosensor. For the identification of microbiological or chemical contamination in food items, the interaction and affinity between the bio-recognition molecule and the contaminant is critical. Many of these bio-recognition molecules, such as proteins (lectins, antibodies, enzymes), and nucleic acids, are found in nature. Other than enzymes and antibodies, lectins are carbohydrate-binding proteins. Lectins are found in many aspects of life, from viruses and bacteria to plants and mammals (Raghu and Kumar, 2020). Lectins are used to detect bacterial infections in food because of their capacity to attach to carbohydrate moieties on bacterial cell walls. Their capacity to distinguish cells has aided in

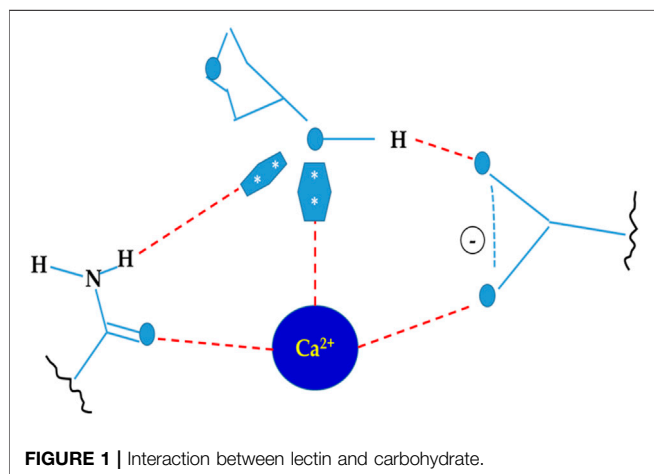
the quick detection of pathogens. Therefore, the use of lectins in the surveillance of food-borne bacterial infections is discussed in this article.

LECTINS

Lectins are usually divalent or polyvalent, with two or more carbohydrate binding sites per molecule. Because each reaction site is capable of connecting to two or more carbohydrates on the bacterial cell surface to generate aggregation and precipitation, they have a one-of-a-kind ability to agglutinate cells. Lectins have multivalent carbohydrate-binding sites that are arranged on the surface. The binding of lectins to carbohydrates involves a variety of chemical interactions, including hydrophobic interactions, hydrogen bonds, van der Waals' interactions, and metal ion coordination (Roy et al., 2016). Hydrogen bonds are mostly formed between carbohydrate hydroxyl groups and lectin protein amine group clusters. Despite the fact that carbohydrates are primarily polar molecules, hydrophobic patches arise as a result of the steric disposition of hydroxyl groups on sugar surfaces, which can interact with lectin hydrophobic areas. Metal ions like Mg^{2+} and Ca^{2+} are found at sugar binding sites of lectins (Figure 1), but they rarely contribute directly to carbohydrate binding (Siebert et al., 2002). The importance of cations in supporting the proper placement of amino acid residues in order to improve interactions with sugars cannot be overstated. Furthermore, water bridges have a role in the interaction between ligands and proteins. Water is analogous to molecular "mortar" because of its small size and ability to operate as both a hydrogen donor and acceptor. As a result, water is crucial in lectin recognition (Slominska-Wojewodzka and Sandvig, 2015).

LECTINS AS BIO-RECOGNITION MOLECULES

Antibodies are commonly utilized in the construction of biosensors to detect food safety risks such as



microorganisms due to their strong and unique interactions. However, there are certain drawbacks to employing antibodies as biosensors for microbial detection in meals, such as the considerable time it takes to separate and refine antibodies. There is also the challenge of regenerating these biosensors, which makes it tough to stabilize the antibodies as part of the lengthy procedure. As a result, using lectins to solve these challenges and detect microbial infections in food is a good idea because lectins are more stable than monoclonal antibodies and there are hundreds of lectins accessible commercially (Masarova et al., 2004).

Because of their high affinity for sugar fractions assisted by polyvalent interfaces originating from the three-dimensional interaction of carbohydrate molecules, lectins make excellent biorecognition molecules. The unique binding of lectins to glycoprotein terminal sugar moieties on cell surfaces has been thoroughly explained (Bertozzi and Kiessling, 2001). **Table 1** lists lectins utilized as bio-recognition molecules, as well as their carbohydrate specificity. Concanavalin A (ConA) is one of the most extensively used lectins in the creation of various sensors for ligand identification using fluorescent markers and fluorometer detection.

APPLICATIONS OF LECTINS IN FOOD SAFETY

Pathogen Separation

Lectins have multivalent and non-covalent interactions with glycoproteins, which are important in distinguishing bacterial pathogens from contaminated food. This feature of lectins has been exploited to isolate gut bacteria by conjugating them with magnetic beads (Gorakshakar and Ghosh, 2016). Lectins have been immobilized on magnetic beads by adsorption, covalent immobilization on tosylactivated beads or biotinylated lectins were coupled to magnetic particles with immobilized streptavidin. Magnetic particles can be separated later using a free competing sugar (Safarik and Safarikova, 1999). A battery of pathogenic and commensal bacteria was tested using lectins extracted from plants such as *Canavalia ensiformis*, *Datura stramonium*, *Vicia faba*, *Solanum tuberosum*, *Helix aspersa*, *Cytisus scoparius*, *Erythrina cristagall*, *Bauhinia purpurea*, *Limulus polyphemus*, *Caragana arborescens*. Lycopersicon Con A lectin, for example, has a higher ability to bind with *E. coli* and *S. aureus* at rates of 0–98% and 50–100%, respectively (Cheung et al., 2015; Malik et al., 2016). Hyun et al. (2020) devised a method for selectively eliminating harmful bacteria by using bacterial lectin-targeting glycoconjugates containing an epitope or a photosensitizer to enhance antibody-dependent cellular cytotoxicity (ADCC) or photodynamic treatment (PDT). Furthermore, Yang et al. (2019a) employed wheat germ agglutinin lectin (WGA) as a bio-recognition agent for *S. aureus* enrichment and found that even at 100–1000 CFU/ml of *S. aureus*, WGA demonstrated high enrichment efficiency. Later, this unique enrichment was applied in a quantitative and selective detection technique to detect *S. aureus* with a detection limit of 3.5 10² CFU/ml using

TABLE 1 | Lectins used in biosensor preparations.

Lectin	Lectin source	Abbrev.	Carbohydrate specificity	Molecular weight
Concavalin A	<i>Canavalia ensiformis</i>	ConA	α -Man, α -Glc	104,000
Dolichos biflorus lectin	<i>Dolichos biflorus</i>	DBA	α -GalNAc	120,000
<i>Erythrina Cristagalli</i> agglutinin	<i>Erythrina Cristagalli</i>	ECA	α/β -GalNAc, α/β -Gal	54,000
Maackia amurensis Lectin (MAA/MAL I)	<i>Maackia amurensis</i>	MAA	α -SA	140,000
Agglutinin	<i>Ulex Europeaus I</i>	UEA I.	α -Fuc	63,000
<i>Sambucus nigra</i> lectin	<i>Sambucus nigra</i>	SNA	α -SA- α -Gal	150,000
Wheat germ agglutinin	<i>Triticum vulgare</i>	WGA	β -GalNAc	36,000
	<i>Galanthus nivalis</i>	GNA	α -Man	52,000
Wheat germ agglutinin	<i>Triticum vulgare</i>	WGA	GlcNAc ₁ -4GlcNAc ₁ -4GlcNAc	34,000

Source: Raghu and Kumar (2020), Raghu (2018), Nand et al. (2014), Mutlu et al. (2008), Masarova et al. (2004).

double stranded DNA (dsDNA) stabilized gold nanoparticles (AuNPs). To improve the efficacy of magnetic nanoparticles in investigating the scope of bacterial pathogen detection based on bio-recognition, a lectin magnetic separation (LMS) technique was developed for *S. aureus* (Yang et al., 2019b) and the main aim was to improve the efficiency of magnetic nanoparticles and to expand the scope of bacterial recognition. In conventional method, i.e., using Baird–Parker (B-P) method, *S. aureus* can be detected at limit of 3×10^0 CFU·mL⁻¹ within 15 h; the polymerase chain reaction (PCR) method can be finished within 4 h, with the limit of detection (LOD) of 3×10^2 CFU·mL⁻¹. The LOD of HRP-pig IgG-based colorimetric method is 3×10^5 CFU·mL⁻¹, and the method only lasts for 2 h. If combined with specific detection methods, it meets different needs for rapid detection of *S. aureus*.

Lectin for *Listeria* spp. Detection

Listeria monocytogenes is categorized into four serological groups and 13 serovars based on somatic and flagellar antigen components (Lopez Valladares, 2019). These are Serogroup 1 (1/2a and 1/2b serovars), serogroup 2 (serovar 1/2c), serogroup 3 (serovars 3a, 3b, and 3c), and serogroup 4 (serovars 4a, 4 ab, 4b, 4c, 4) (Li et al., 2020). Nonetheless, epidemiologic studies benefit little from serotyping because only three serovars, 1/2a, 1/2b, and 4b account for over 90% of all clinical isolates (Braga et al., 2017). Changes in glycosidic substituents coupled to a polyribitol phosphate (Rbop) backbone cause the most variation in wall teichoic acids (WTA) (Brown et al., 2013). WTAs in *L. monocytogenes* are made up of repetitive Rbop units with variations in carbohydrate molecules such as galactose, rhamnose, glucose, and N-acetyl glucosamine, which vary a lot according to the strain and serovar. On the C-2 and C-4 sites of the thiol group, serovars 12 and 3 have rhamnose sugars and GlcNAc. Serovars 4, 5, and 6 have a more complex WTA assembly in the centre of the GlcNAc chain, which is fused as a chunk of the polyribitol chain and may contain Glc and/or Gal substituents. *Listeria* WTA does not have any D-alanine substituents (Bielmann et al., 2015). Through a GlcNAc moiety, wheat germ agglutinin (WGA) binds to WTAs (Murakami et al., 2014). Flannery (2019) used an agglutination assay and a fluorescence-based assay to investigate cell wall diversity of *Listeria* spp., *Canavalia*

ensiformis, *Griffonia simplicifolia* lectin I, *Helix pomatia* agglutinin, *Ficinus cummunis* agglutinin, and *Ricinus communis* agglutinin in clinical, food, and environmental isolates.

Agglutination Reaction of Bacteria on Lectin-Labeled Magnetic Beads

Sun et al. (2017) isolated and separated enteric bacteria using lectin-labeled magnetic beads. They utilised sixteen different types of lectins and found that magnetic beads labelled with Con A produced the most agglutinations **Figure 2**. From river water and laboratory cultures, this approach could extract pure and culturable cells. The findings are equivalent to those obtained using antibody-labeled beads. The findings are encouraging, implying that lectins could be employed as an alternate cell discriminator. Sun et al. (2017) separated coliform from fresh water and effluent from a water treatment plant using lectin-labeled magnetic beads. Direct magnetic capture was shown to be less reliable than indirect magnetic capture. Harito et al. (2017) employed the lectin magnetic separation (LMS) approach to isolate *Toxoplasma gondii* oocysts from water sample concentrates, with microscopy or molecular methods used for identification. Castillo-Torres et al. (2019) used lectin-functionalized and aptamer-functionalized microdiscs to demonstrate selective separation of generic coliforms and *E. coli* cells, respectively. They also discovered a direct association between bacterial concentration and low signal in control samples in the form of fluorescence signals, which are directly correlated to bacterial concentrations and visible in control samples (negative samples). Using Con A-linked magnetic beads to detect Hepatitis A Virus (HAV), Ko et al. (2018) discovered that it had a significantly higher binding affinity for HAV than reverse transcriptase PCR, with a detection concentration of 10^{-4} of the virus stock. Magnetic beads containing fragment crystallizable-mannose-binding lectin (FcMBL) were used to capture and magnetically remove bacteria from purified cultures of 12 *S. aureus* strains, as well as from 8 articular fluid samples and 4 synovial tissue samples collected from patients with osteoarthritis or periprosthetic infections at 85% efficiency (Bicart-See et al., 2016). Tateno et al. (2018) employed lectin to bind malignant

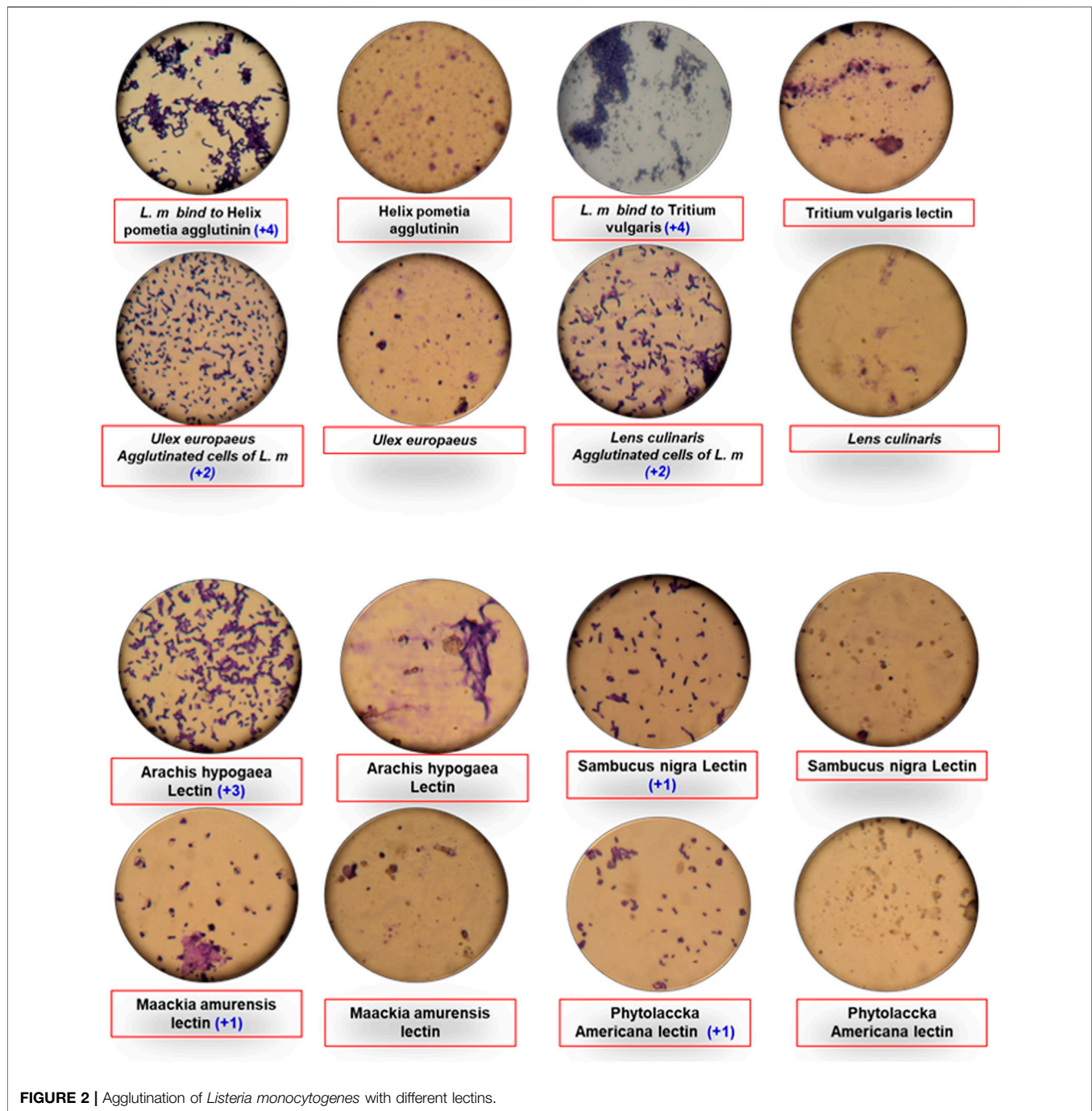


FIGURE 2 | Agglutination of *Listeria monocytogenes* with different lectins.

cells based on cell agglutination, which resulted in cell death, according to a US patent.

FLUORESCENCE BASED BIOASSAY

Flow Cytometry Methods

Hendrickson et al. (2019) used a ligand–bioreceptor interaction to develop a flow cytometer analysis of the bacterial pathogens *E. coli* and *S. aureus*. Plant lectins with fluorescent labels were

used as natural receptors that could precisely bind with bacteria's cell wall polysaccharides. Additionally, epifluorescence microscopy was employed to validate and observe lectin–carbohydrate interactions. The binding specificity of plant lectins to *E. coli* and *S. aureus* cells was investigated, and wheat germ agglutinin was chosen as a receptor since it provided high-affinity interactions. Bacterial pathogens can be detected up to 10^6 cells/mL in 5 min using this approach. Lectin reagents are a promising method for controlling a wide spectrum of bacteria due to their accessibility and universality.

TABLE 2 | Application of lectins in the development of biosensors.

Type of biosensors	Name of lectin	Pathogen	Sensitivity	References
Electrochemical sensors	Lectin	<i>Bacillus cereus</i> , <i>Staphylococcus aureus</i> , <i>E. coli</i>	—	Thevenot et al. (2001)
	Lectin	<i>E. coli</i>	—	Ertl and Mikkelsen, (2001)
Flow cytometry	Con A	<i>Candida species</i>	10 ² –10 ⁵ cfu/ml	Sa et al. (2020)
	<i>Hechtia argentea</i>	<i>Salmonella species</i>	5 cfu/ml	Lopez-Tellez et al. (2020)
	WGA	<i>E. coli</i> O157:H7	102 cfu/ml	Li et al. (2015)
	Con A	<i>E. coli</i>	75 cells/mL	Yang et al. (2016)
	WGA	<i>E. coli</i> and <i>Staphylococcus aureus</i>	10 ⁶ cfu/ml	Hendrickson et al. (2019)
Paper based sensors	WGA	<i>Listeria monocytogenes</i>	1 × 10 ⁶ cfu/ml	Raghu (2018)
Piezoelectric biosensors	Con A	<i>E. coli</i>	1 × 10 ⁴ cfu/ml	Serra et al. (2008)
	Con A	<i>E. coli</i>	100 cfu/ml	Shen et al. (2007)
	Con A	<i>Campylobacter jejuni</i>	—	Yakovleva et al. (2011)
Porous silicon-based biosensor	Con A	<i>E. coli</i>	10 ³ cfu/ml	Yaghoubi et al. (2020)
	WGA	<i>S. aureus</i>	—	—
Quartz crystal microbalance (QCM)	Con A, <i>Ulex europaeus</i> , <i>Maackia amurensis</i> , <i>Lens culinaris</i> , wheat germ agglutinin	<i>Pathogenic Bacteria</i>	10 ³ cfu/ml	Safina et al. (2008)
	WGA	<i>E. coli</i> O157:H7	3 × 10 ³ cfu/ml	Wang et al. (2013)
SPR	WGA	<i>Listeria monocytogenes</i>	1 × 10 ³ cfu/ml	Raghu and Kumar, (2020)
	Fimbrial lectin	<i>E. coli</i>	1 cfu/ml.	Yazgan et al. (2014)

Fluorometer Based Methods

The inclusion of 4 tryptophan, 12 cysteine, and glycine residues in the amino acid sequence of wheat germ agglutinin (WGA) may explain its natural fluorescent ability (Bogoeva et al., 2004). WGA has a characteristic tryptophan emission at 348 nm in its fluorescence spectra. The results of the fluorescence study led to the conclusion that fluorescence and phosphorescence are caused by at least two of the three tryptophan residues in WGA (Liener, 2012). With increased amounts of log cfu/ml of *L. monocytogenes* cells, the binding constant of WGA was increased. The affinity of carbohydrate binding domains (CBDs) to their carbohydrate ligands is equivalent to affinity-matured antibodies to bacterial cell surface antigens (Bi and Zimmer, 2020). Another study by Loessner et al. (2002) found that at increasing carbohydrate concentrations, CBDs have a higher association constant with their carbohydrate ligands. Another study found that *E. coli* O157:H7 that binds to lectins had a higher association constant (K_a) (Wang et al., 2013). In the presence of particular sugar and *L. monocytogenes*, Raghu (2018) detected maximum fluorescence in the spectra using 290 nm as excitation and 350 nm as emission wavelength with increasing WGA concentration. Therefore, the principle of WGA fluorescence could also be a technique for developing fluorometric tools for detecting *L. monocytogenes*.

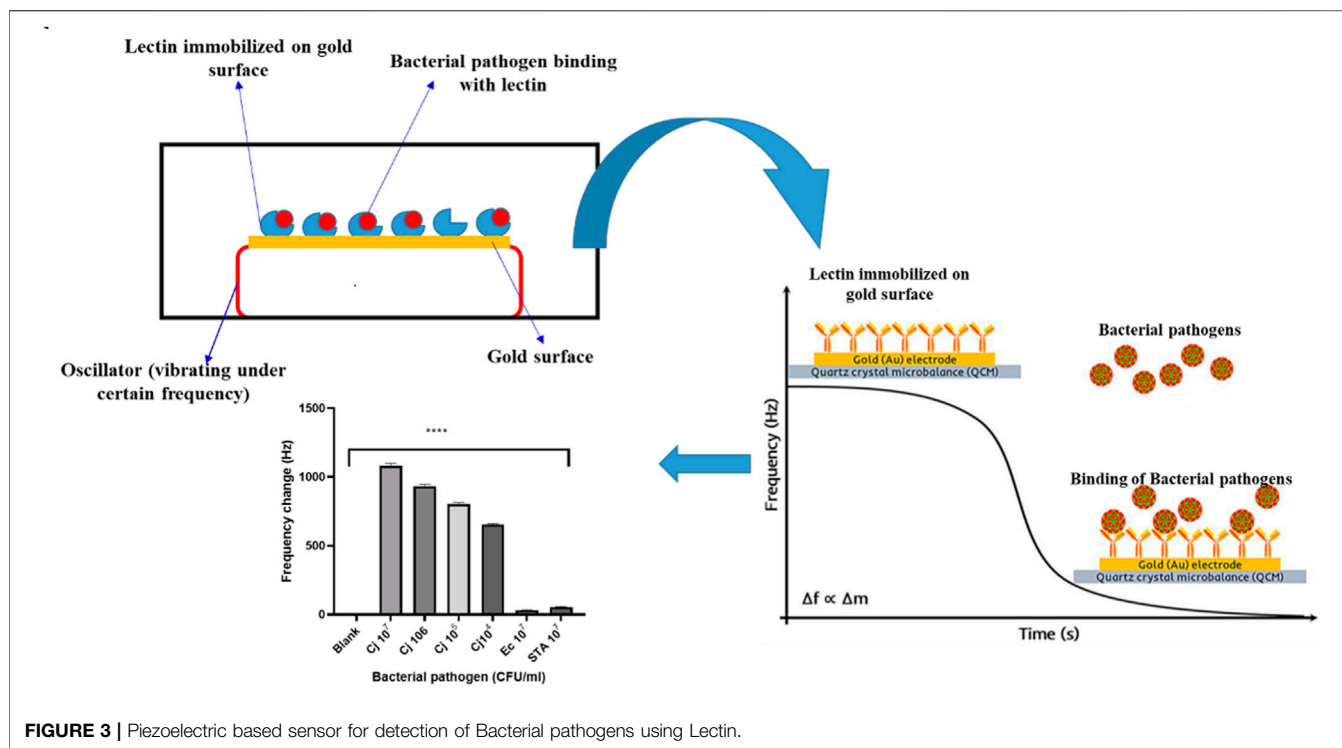
Lectin-Based Biosensors

Using platforms such as electrical oscillation (Bhalla et al., 2016), piezoelectric crystal, and micro-calorimetrics, several modules of lectin-based biosensors have been constructed (Vereshchagina et al., 2015). **Table 2** shows an overview of biosensors created for the detection of infections employing lectins. Biosensors are seen as a promising alternative to the traditional procedures that have

been used in the past. The biorecognition element must be fixed on the sensor surface to provide high selectivity. Lectins are a type of biorecognition element that is more stable and covers greater surface area than other biomolecules like antibodies (Sondhi et al., 2020). The sections that follow will go over the many types of transducers that can be utilized to detect bacterial infections using lectins.

Piezoelectric Biosensors

Piezoelectric biosensors are analytical devices that work on the idea of analyte and ligand molecule affinity, which causes a change in mass/weight on vibrating quartz crystals, changing the frequency of oscillation. The change in oscillation frequency is a measure of the analyte concentration in the samples (Skladal, 2016), and **Figure 3** is a graphical depiction of a piezoelectric lectin-based sensor. A weight indicator made from a vibrating quartz crystal is extremely sensitive and accurate. Mass changes can be detected utilizing a crystal-controlled oscillator and the piezoelectric biosensor's resonance frequency (Petr, 2015). Serra et al. (2008) suggested a piezoelectric biosensor for the detection and quantification of bacteria using an electrochemical quartz crystal microbalance (EQCM). Con A and *E. coli* were used to test the efficacy of lectin-based quartz crystal microbalance. Shen et al. (2007) employed a non-labeled quartz crystal microbalance (QCM) biosensor to detect bacterial infections using lectins as bio-receptors. The bio-recognition of O-antigen using a carbohydrate non-labeled mass sensor packed with lectin could be a promising technique with a reduced detection limit and maximum selectivity for high molecular weight bacterial targets. With the use of Con A lectin as the bio-recognition molecule, Shen et al. (2007) developed a QCM biosensor. It did, however, reveal a low detection limit for *E. coli* (limited to a few hundred bacterial cells). These proteins were employed by Serra



et al. (2008) to make biosensors for detecting bacterial infections. Using an EQCM, gold-plated quartz crystals were immobilized with lectins. The Con A was used to test the efficiency of the lectin immobilization approach and the biosensor performance for *E. coli* detection. Adsorption of polarized and non-polarized (0.200 V) gold-empeneled quartz crystals through avidin–biotin binding was used to ensure attachment of Con A. By measuring the change in frequency with *E. coli* concentration 1 h after bacterial binding, a linear calibration plot in the range of 5.0×10^6 to 2.0×10^7 cfu/mL was obtained, with the limit of detection of this developed sensor at around 1.0×10^4 cfu/mL.

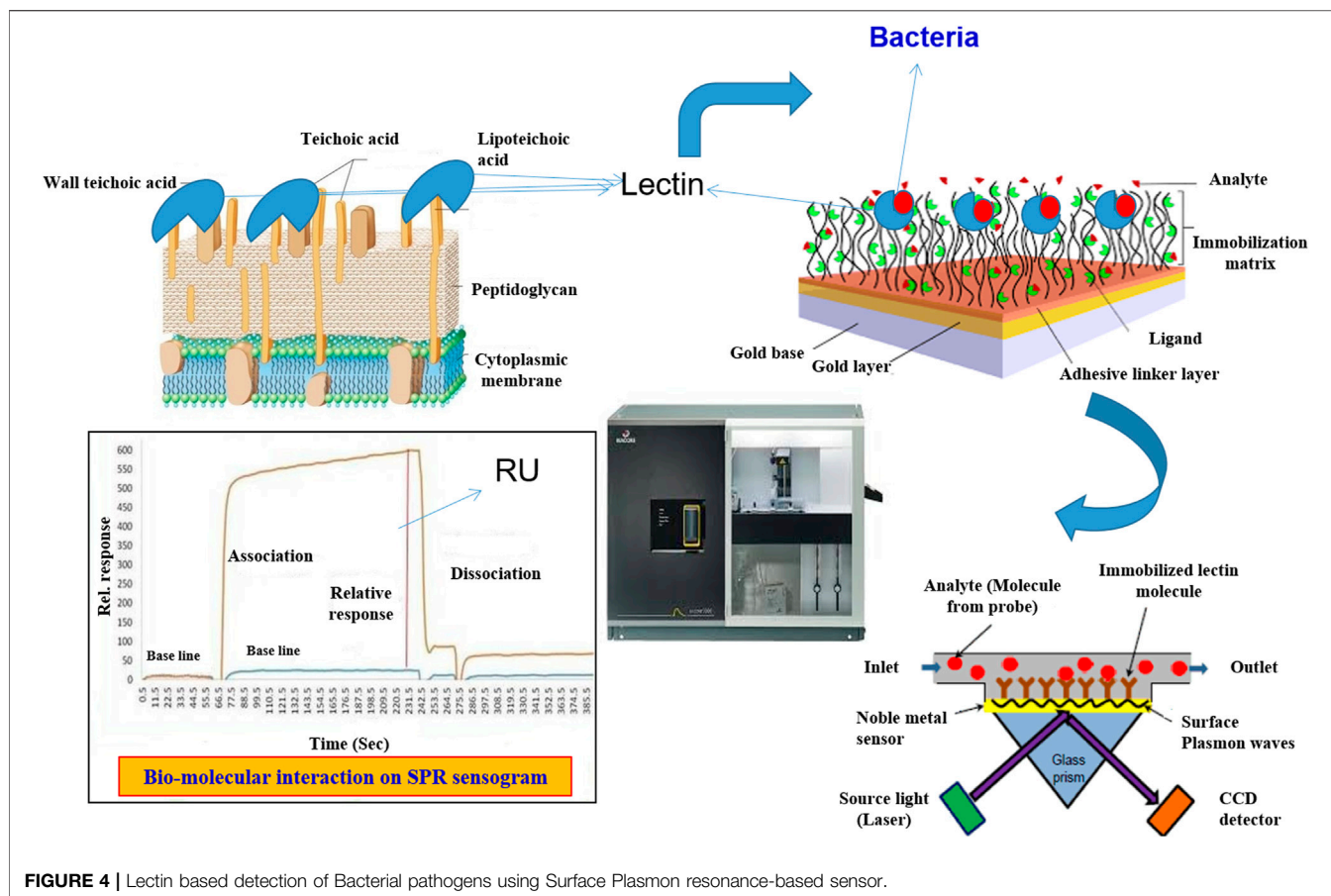
Using four different carbohydrate binding lectins, namely WGA, MAL, LCA, and Con A, a QCM biosensor was applied to distinguish seven *Campylobacter jejuni* strains (Yakovleva et al., 2011). The frequency change in the Con A lectin was higher at 34 Hz (Wang et al., 2013). The use of a carbohydrate epitope in conjunction with a lectin–bacterial O-antigen interaction in the development of sensitive and specific non-labeled biosensors for the detection of bacterial pathogens has been demonstrated using this patented technology for “Microorganism Detection and Analysis Using Carbohydrate and Lectin Recognition” (Zeng and Shen, 2016). Many other exo- or endogenous toxins produced by or present in bacterial cells may detect the carbohydrate ligand and generate increased cross-reactivity, leading to false positive and negative results.

Surface Plasmon Resonance Biosensor

Liedberg was the first to propose the SPR sensor for use in biosensors (Prabowo et al., 2018). It has now been thoroughly investigated and is gradually evolving into an inherent label-free

device for facilitating chemical interactions between the target analyte and ligand molecules. When a photon of light strikes a metal surface (gold or silver), it interacts with and excites the metal’s electrons, causing them to move as a single electrical unit called a Plasmon, which oscillates parallel to the metal surface (Mitchell and Wu, 2010). Surface Plasmon is a phenomenon in which a Plasmon oscillates and generates an electric field that extends about 300 nm out from the metal surface (Homola, 2003; Hoa et al., 2007). It is based on the fact that at a specific incidence angle and wavelength, electrons in a metal layer become excited and absorb light. Surface Plasmons (SPs) are electron density waves that develop at the interface of a metal (such as gold) and a dielectric (such as glass). Changes in the refractive index caused by an analyte binding to a prism’s metal-coated surface characterize these waves (Mullett et al., 2000; Homola, 2003). A resonance occurs at a specific angle where the energy shift from the photon to the Plasmon is well matched, resulting in significantly increased energy shift and a commensurate decrease in reflectance (Mitchell and Wu, 2010).

If mass is attached to the surface within this 300 nm region, it perturbs the Plasmon and alters the resonance angle for a photon of fixed wavelength. If the metal surface’s plane is fixed, the resonance wavelength can be determined by scanning a range of photon incidence angles and determining the resonance angle (Zeng et al., 2017). An SPR biosensor operates on the same concept as a surface Plasmon resonance sensor, measuring minute changes in refractive index that correspond to binding interactions on the sensor surface (Homola, 2008). In most cases, SPR biosensors can achieve resolutions of 1 resonance unit (RU), or 1×10^{-6} refractive index units (Prabowo et al., 2018). SPR biosensors can detect binding interactions between molecules as



small as 2 kDa, but smaller molecules produce insufficient changes in bound mass, which cannot be monitored directly (Perumal and Hashim, 2014).

Only a few reports on how lectins are employed as a bio-receptor for bacterial detection are available to date. Gram-negative bacteria, such as *E. coli*, can be distinguished by their chemically distinct surface LPS, which can be detected by specific lectins; hence, bio-receptors assist ConA attach to *E. coli* W1485. Masarova et al. (2004) created a SPR detection system for endotoxins or entire bacterial cells by covalently attaching eight distinct lectins to CM 5 chip surfaces (CM5). These eight lectins were found to be unique. Based on lectin-endotoxin (lipopolysaccharide) interaction, these eight lectins were able to distinguish between the microorganisms. Wang et al. (2013) employed SPR to create a novel type of biosensor for detecting *E. coli* O157:H7, which utilized lectin as a bio-recognition molecule. Using amine coupling chemistry, lectin was immobilized on the gold chip (CM5) surfaces to capture this bacterial pathogen in the buffer solution. WGA, ConA, UEA, PNA, and MAL were evaluated for the best lectin, one that could efficiently bind to this bacterial pathogen. Among the lectins that were screened, WGA lectin has a wide linear range of 3×10^5 to 3×10^8 cfu/mL with a lower detection limit of 3×10^3 cfu/mL, demonstrating good selectivity by utilizing SPR. SPR has advantages over QCM and electrochemical measurements,

according to Raghu and Kumar (2020). This is because biomolecular interactions can be tracked in real time, allowing kinetic parameters to be determined (KD and KA). The affinity constant KA, in particular, aids in performance analysis of the bacteria and carbohydrate binding protein in terms of specificity and utility. In contrast, there are few publications on lectin based SPR sensors. Wang et al. (2013) and Raghu and Kumar (2020) developed a novel SPR biosensor using lectin as the bio-receptor for fast detection of *E. coli* O157:H7 and *L. monocytogenes*. **Figure 4** depicts the sensor configuration for the detection of *L. monocytogenes*. Lectins were immobilised on the CM5 chip with the help of self-assembly monolayers to capture *E. coli* O157:H7 in the buffer solution (SAM). In another investigation, Leonard et al. (2004) used a Biacore SPR 3000 biosensor with a detection limit of 1105 *L. monocytogenes* cells/ml within 30 min to detect *L. monocytogenes* with a polyclonal antibody.

Electrochemical Sensors

An electrochemical sensor is a device that turns biological events into a signal that can be measured analytically, such as the amount of a certain analyte in a sample or composition, harmful contaminants, or bacterial infections (Thevenot et al., 2001). A distinguishing feature of an electrochemical biosensor is the electrochemical technique used. By using lectins as a bio-recognition molecule, Ertl and Mikkelsen (2001) produced an

electrochemical biosensor array, and transduction is assessed by taking the respiratory cycle activity, in which the native respiratory chain of the microbe is interrupted by exogenous oxidants. They discovered a link between agglutination outcomes and the electrochemical assessment of lectin cell binding. To determine how each organism reacts to lectin, chronocoulometric measures were created. *Bacillus cereus*, *S. aureus*, *Proteus vulgaris*, *E. coli*, *Enterobacter aerogenes*, and *Saccharomyces cerevisiae* can all be distinguished using the established method. Ertl et al. (2003) also created an electrochemical biosensor with a screen-printed array whose selectivity was based on lectin affinity for cell-surface lipopolysaccharides. These arrays were used in conjunction with factor analysis to quickly identify four *E. coli* subspecies (*E. coli* B, *E. coli* Neotype, *E. coli* JM105, and *E. coli* HB101) in under 40 min (Velusamy et al., 2010). Sa et al. (2020) used Con A and WGA to construct an impedimetric biosensor for detecting pathogenic *Candida* species. The sensor can distinguish between *Candida* species with a detection sensitivity of 10^2 – 10^6 CFU/ml. Lopez-Tellez et al. (2020) established a sensitive electrochemical detection approach for *Salmonella spp.* employing Hechtia argentea lectin immobilized on a screen-printed gold electrode that exhibited selectivity for D-mannose, which is found on the lipopolysaccharide (LPS) layer of *Salmonella spp.* With increased concentrations of *Salmonella spp.*, the interaction of bacteria with immobilized lectin on a biosensor surface increased the impedance, achieving a detection range of 15 – 2.57×10^7 CFU/mL, with a 5 CFU/ml limit of detection.

Limitation of Biosensors

Lectin biosensors have a limited ability to work in a multiplexed fashion, which is their principal drawback. Only SPR imaging (SPRi) and, to a lesser extent, micro-cantilever-based assays allow for highly parallel analysis. More research on electrochemical approaches that work in an array arrangement is required. It is expected that lectin biosensors will be better suited for diagnostic purposes than for preliminary assays of a large number of samples. There is also the additional problem of lectin biosensors and their use in the examination of real complex materials (Belicky et al., 2016). However, controlled immobilization of lectin for the construction of lectin biosensors is more difficult due to the larger complexity of a protein molecule.

Future Prospectus

Carbohydrate-protein interactions have been identified as critical for a variety of biological activities, including extracellular and intracellular signaling, as well as cell-to-cell recognition. Lectins are useful tools for studying glycoconjugates and understanding the mechanics of numerous biological processes because of their carbohydrate binding selectivity. Lectins are useful tools in glycobiology and are the greatest model system for studying protein-carbohydrate interactions. Lectins have been linked to the creation of lectin-based high-throughput molecular tools and have established themselves as a major glycan decoding

tool in glycobiology. However, there is still a lot of room for lectins to be used in numerous biotechnological and medicinal applications. Furthermore, the identification and characterization of novel lectins, as well as in-depth research on existing lectins, will have a significant impact on future research.

CONCLUSION

The right to food and the right to safe food are two sides of the same coin; one without the other is incomplete. Food security and delivering safe food to consumers are becoming increasingly important to all food supply chain stakeholders. This has turned the focus to developing accurate, precise, and cost-effective quick food pathogen detection systems with an ergonomic design. The search for an effective biosensor has led to the discovery of a number of bio-recognition molecules with excellent specificity and sensitivity. Antibodies performed admirably; however, they have intrinsic limits in terms of synthesis. Sugar binding proteins, such as lectin, have emerged as potential alternatives to antibodies due to their high specificity, abundance, and stability. It is a positive development that lectins can act as bio-receptors in a number of biosensor systems. As a result, lectin research has received a lot of attention, and scientists all over the world are attempting to fully exploit this new line of biosensor technology. These lectins have found widespread application in clinical settings, generating hopes for their potential use in rapid pathogen detection systems in disease diagnostics and food safety. Lectins have been linked to the creation of lectin-based high-throughput molecular tools and have established themselves as a major glycan decoding tool in glycobiology. Furthermore, the identification and characterization of novel lectins, as well as in-depth research on existing lectins, will have a significant impact on future research. Despite some progress, more effort is required to fully realize the potential of lectins as biosensors.

AUTHOR CONTRIBUTIONS

RV and ST wrote the introduction, lectins, types of lectins, biological significance of lectins, bio-recognition molecules, application of lectins in detection of pathogens, lectin-based biosensors, and lateral flow assay. KG, BC, and CH drafted the introduction, conclusion, and references. NK, AP, and RA provided direction and critically revised and edited the manuscript. The final version was approved by all authors.

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