Halal food authentication platforms: Potential and perspective in nanotechnology

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Abstract

The authentication of food is a vital part to ensure quality foods in compliance with fair prices and religions. Furthermore, the newly emerging "zoonotic" disease threats those are capable of being transmitted from animal to human has added enormous drive towards meat species and food quality authentication. However, individual consumer cannot verify the quality attributes of processed foods using organolaptic test or even after consumption of food. Therefore, "Halal" logo in food products signifies the preparation of food with ingredients according to Islamic shariah and denotes its value for religious faith and hygiene. Hence, many countries including Malaysia, Indonesia, Thailand, Singapore, China, Brazil, Australia and New Zealand are having regulatory bodies to ensure proper labelling of Halal status of raw and processed foods. For food authentication, DNA based method gains much interests due to its stability under different food processing conditions and certain assays including Polymerase Chain Reaction (PCR) have been proposed. Along with PCR, nanotechnology came forward with utilization of optical, electrochemical screening approaches for halal authentication based on bio-recognition events on solid devices and in solutions with better accuracy and sensitivity. These novel nano-platforms build various DNA reorganization tools combining the spectroscopic, electrochemistry, magnetic and other analytical field. Nanoparticles coupling with specific DNA molecule can recognize bioactive substances and allow real-time monitoring. Furthermore, surface-enhanced Raman scattering (SERS) allow rapid label-free detection of small DNA target for halal to homeland security. SERS provides a highly sensitive nano-platform for halal authentication with "fingerprinting" ability to produce distinct spectra from molecules similar in structure and function. It eliminates the use of expensive reagents or time-consuming sample preparation steps associated with traditional detection techniques. In addition, extrinsic

SERS detection can provide further advantages of multiple detections with single source laser excitation with non susceptible photo bleaching effect.

Keywords: Halal authentication, Meat, Food, Nanomaterials, SERS, nanobiosensor.

1. Halal Food and Authenticity Issue

In tandem with massive attention given to halal industry, global halal market nowadays appeared to be one of the fastest growing business sectors in the world as they estimated to worth more than USD2.3 trillion (World Halal Forum, 2013). The definition of halal itself is any things that permissible by Shariah rulings (Islamic law), therefore it can be classified in several forms; food (nourishments, medicines), non-food (cosmetics, healthcare) and services (banking, trades and logistics) (Che Man, 2010). Focusing on the food sector, it contributed approximately USD700 billion to global halal industry in order to fulfil the requirement of nearly 1.8 billion Muslim population in the world (World Halal Forum, 2013). The rising of Halal food demand represents the consumer's trustworthy to the authorities to serve the best for them which include the sources, cleanliness, and ingredients.

According to Hargin, 1996, non-authentic food can be defined as food which is not of the nature or substance or quality demanded by the consumer. They can be either omission of valuable components, substitution of undeclared cheaper materials, concealment of foodstuff or addition of undeclared product bulk in order to increase the commercial value. In most countries, food manufactures choose to use porcine derivatives because they are cheap and readily available (Aida, Che Man, Wong, Raha, & Son, 2005). However, pork is no longer the only option nowadays. Mammals like cat, dog or even rats were being use as meat substitute as they can be found easily at the alley. Wildlife animals such as macaque has a high potential to become adulterant since their population are very huge and easily obtain in the city.

Modern and busier current lifestyle require consumer to pick something that easier and quick to be served, hence, the processed food/meat is much preferable for them. However, the mislabelling and fraudulent often happens in this industry due to high-competitions and

profit-gaining among the food company (Ali et al, 2012b). Most recent cases regarding food adulteration has been reported in 2013, such as horse meat scandal in beef product across Europe (BBC News,2013a) and pies which claimed "halal" but apparently contain pork as servings for Muslim prisoners in UK (BBC News,2013b). Due to myriad food authentication issues, consumer became highly selective on the food and really concerned about the labelling on the package not only because of religious, but also to prevent from any severe disease and allergies (Ballin, 2010; Ali et al., 2012b). The protection of endangered aquatic and wildlife in natural habitats is also relevant to meat authentication (Ali et al. 2012c; Fajardo et al. 2010).

Inspired by the urge transparency in food industry, scientists has developed many techniques from different approach for identification of meat species in either raw or processed ones (Cozzolino & Murray,2004; Che Man et al. 2007; Ghovvati et al.,2009; Soares et al., 2010; Karabasanavar et al., 2011, Ali et al. 2011a, b, 2012a;; Haider et al.,2012). Many countries including Malaysia, Indonesia, Thailand, Singapore, China, Brazil, Australia and New Zealand are having regulatory bodies to ensure proper labelling of Halal status of raw and processed foods. Thus, an easy user friendly and improved authentication techniques for "Halal" verification brands is vital for food manufacturers, marketers and regulators.

2. Analytes for Halal food authentication

Labeling of the products need to be varified for true content of the foods with a sensitive, easily performable and reliable scientific method. The call for accurate and reliable methods for animal species detection has tremendiously step forwards during past decades for certain issues. For example, halal authentication along with recent food alert (e.g.avian flu), misconduct of some manufacturter, genetically modified product and food alllergies have immensely reinforced public responsiveness abut the components of the food (Teletchea et al., 2005). Thus numerous technically consistent analytes based on lipid, protein and DNA are proposed for detection of animal species in food (Nakyinsige et al., 2012). The field of these analytes for food authentication and the turning point have been represented here.

2.1 Lipids

In food species detection, lipid-based methods are based on the positional analysis of fatty acid in triacylglycerol (TAG) and 2-monoacylglycerol (2-MAG). For example TAGs analysis of certain species like extensively farmed pig, wild boar, red deer, rabbit, and goose showed stored monoenoic and n-6 polyenoic acids with higher chain length and unsaturation (except pig) at sn-2 position. But the major draw backs of the species-specific analysis of the positional distribution of fatty acid is that the contents and varieties of TAGs and MAGs can be altered by the food cooking process (Ali et al., 2012b). Hence, in food species authentication the lipid-based recognition tools have narrower applications. However, for discrimination of animal and plant originated fats the fatty acid composition analysis is a useful marker. To detect the replacement of vegetable oils with lower costing lard in Halal, Kosher, and vegan food products analysis of fats and fatty acid compositions by FTIR spectroscopy combined with multivariate partial least square fit (PLS) or principal component analysis (PCA) (Rohman et al., 2011) or electronic nose coupled with gas chromatography-mass spectrometry are useful approaches (Ali et al., 2012b).

2.2 Protein

In food species detection, the usefullness of species specific protein analysis by utilizing electrophoretic (Montowska and Pospiech, 2010), chromatographic (Chou et al., 2007) and spectroscopic (Ellis et al., 2005) tools have been documented. But the potential of protein based approach have been restricted due to the denaturation of soluble protein under thermal treatment, specially in food processing steps. Furthermore, analysis of antibodies raised against a specific protein by immunoassays have the possibiliy to interupt by the cross-reactions of the closely related species, leading to descremination failure (Ayaz et al., 2006).

2.3 DNA

Recent DNA based analytical platform showed huge potential to food manufactures, researchers, and regulators for qualitative and quantitave analysis of processed food ingredients. In finished commercial products, to identify the declared or undeclared ingredients, DNA-based method is effecient to detect a small level of adulteration in process foods. Thus the invention of different Polymerase Chain Reaction Assays based on species

specific DNA fragemnt analysis exploit the transparency and fair-trade in food industry (Ali et al., 2013).

3. PCR in Halal Authentication

PCR, an acronym for Polymerase Chain Reaction (Mullis and Faloona, 1987) is an *in vitro* amplification procedure from a specific DNA template to large quantities from a complex pool of DNA using a simple enzymatic reaction. PCR come forward for Halal authentication through detection of specific DNA target from certain species as a simple and useful laboratory tool.

3.1 General Principles and reaction specificity of the PCR

For specific DNA detection with simple PCR assay, oligonucleotide primers are designed targeting the complementary sequence at the ends. Admixture of the primers with DNA template, deoxyribonucleotides and suitable buffer followed by heat treatment denature the original strands. Further cooling promotes primer annealing and by the action of DNA polymerase and new strands is synthesized. New copies of DNA are formed by repeated cycle of denaturation, annealing, and polymerase action. Finally an exponential increase in the total number of specific target DNA occur with a theoretical abundance of 2n, where n is the number of cycles (Figure 1) (Erlich et al., 1991).

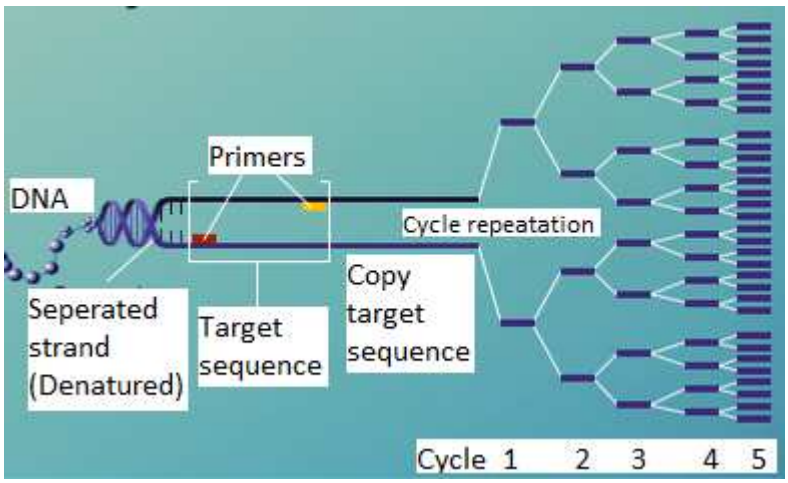

Figure 1: Specific DNA target replication by PCR

3.2 Advantages of PCR

***Easy and fast**:* DNA cloning by PCR around 30 cycles containing a denaturation, synthesis and re-annealing step can be performed using relatively short amount of time than other methods. It is easy to set up a PCR reaction with thermal instrumentation facilitated by gradient PCR machine. . Furthermore PCR assay is forwarded by development of computer based primer designing and oligonucleotide synthesis by commercial or academic bodies (Erlich et al., 1991).

***Highly Sensitive**:* PCR is able to amplify specific DNA target from minute amounts of DNA even from a single cell (Li et al., 1988). Such superb sensitivity opened up the opportunity for utilization of PCR for Halal authentication from trace amount DNA from highly process food even up to 0.01 % of non halal adulteration (Figure 2).

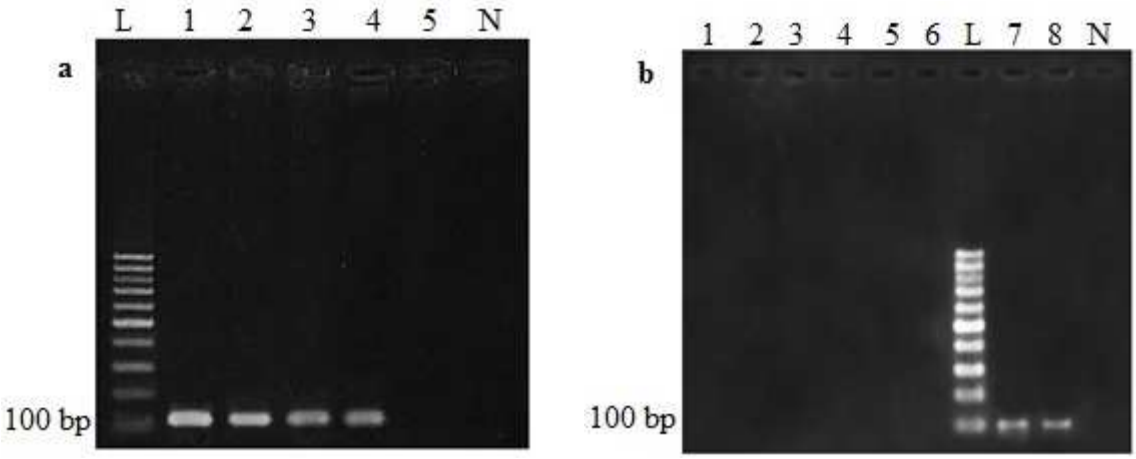

Figure 2: Halal food authentication (Frankfurter) using mitochondrial cytb based (100 bp) canine specific PCR assay with 0.1% sensitivity. **a** 100 bp PCR products obtained from 10%, 5%, 1% and 0.1% of dog meat spiked dummy chicken frankfurters. Lane: 1-5: 10%, 5%, 1%, 0.1% and 0.01% dog meat spiked dummy chicken frankfurters respectively; Lane N: negative control. **b** No PCR product was obtained from commercial frankfurters except from 0.1% dog meat spiked chicken and beef dummy frankfurters. Lane 1-3: commercial chicken frankfurters; Lane 4-6: 1-3 commercial beef frankfurters purchased from Malaysian local market. Lane L: 100 bp Ladder; Lane 7 and 8: 0.1% spiked chicken and beef frankfurter respectively; Lane N: negative control

***Robustness**:* The PCR assay can be performed from a range of nucleic acid sources. The suitable templates for PCR amplification may vary from purified DNAs from various species to specific sequences from material in which the DNA is badly degraded or embedded in a medium from which conventional DNA isolation is problematic. Therefore, PCR platform can recover and amplify the species specific DNA target from a few copies to easily detectable quantities, even from a highly degraded samples and complex pool of DNAs (Ali et al., 2012a).

3.3 Limitations of PCR

Although PCR is a popular technique for routine analysis but it has certain draw backs for selective amplification of specific DNA target. In PCR, for specific target detection and construction of a specific oligonucleotide primer prior sequence information is necessary. Furthermore for highly process food analysis or short length DNA target analysis <36 bp PCR is not efficient due to the requirement of primer length, where forward and reverse should be >36 bp with better specificity.

4. Potential of Nanotechnology for Halal authentication

Nanotechnology is the creation of USEFUL/ FUNCTIONAL materials, devices and systems of any useful size through control and/or manipulation of matter at the nanometer length scale. Its introduces novel phenomena and properties (Physical, Chemical, Electrical, Mechanical, Optical, Magnetic) which arise because of the nanometer length scale. Development of nanotechnolgy aimed to understand and control matter at dimensions of approximately 1 - 100 nanometer. Nanotechnology facilitates understanding, creation, and use of structures, devices and systems with fundamentally new properties and functions because of their nanoscale structure.

Ample analysis of process food in the last decades imitated the usefullness of DNA as the most stable biomolecule for animal species authentication for raw as well as commercial products for animal-derived materials. Latest nano-platform come forward with attractive nanomaterial with excellent physio-chemical properties to create building block for DNA molecule reorganization. Nanoscientists have ascertained the characteristic of certain

nanomaterials (1–100 nm) exibiting increased surface to volume ratio with nanoscale dimensional change with more specific application. Traditional DNA recognition techniques based on PCR assays specially for quantitative analysis are suffering for the need of costly instruments and reagents along with photo-bleaching effect (Tansil and Gao, 2006). Nanoplatform come forward with its strong promise of solving these delicate human problems with the maximum efficiency with minimum cost and time.

5.Nanotechnology in sensor development for Halal food Authentication

5.1 Componets of a biosensor for Halal food authentication:

Biosensor is a device which involves incorporation of bioactive material with transducing element for detecting the concentration or activity of analyte present in the sample. There are three major components for a typical biosensor, 1) Biologically active material or biological recognition element or receptor; 2) Detector element or transducer, and 3) Signal processor. The fisrt component is the target binding molecule. Therefore, for Halal authentication the target biological component of the food must be highly specific, stable under storage conditions, and fixed. Hence, DNA based sensor will facilitate the specificity and stability of the sensor. The second component with nanomaterial incorporation will facilitate the interface, measuring the physical change that occurs with the reaction at the bioreceptor then transforming that energy into measurable electrical output. The third component forward signals from the transducer to a microprocessor where they are amplified and analyzed. Thus the prototype of a DNA based sensor for halal authentication is included in Figure 1.

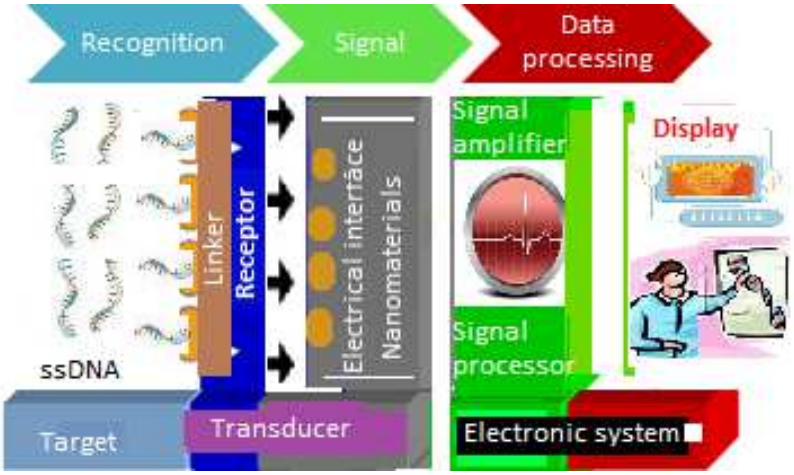

Figure 3: Nanoparticle based halal authentication sensor

5.2 Immobilization of recognition elements for Halal authentication

DNA probes with shorter target represents the most effective biological recognition elements for halal authenticaion. Thus immobilization of DNA with nanomaterials is vital for the development of a biosensors with increase sensitivity. To accomplish high sensitivity and selectivity, it requires minimal nonspecific adsorption and stability of immobilized biomolecules. DNA can be immobilized on biosensor surfaces though adsorption, covalent immobilization by carbodiimide (EDC) coupling, thiol modification with nanoparticle (AuNMs) (Figure 4), and avidin (or streptavidin)-biotin interaction.

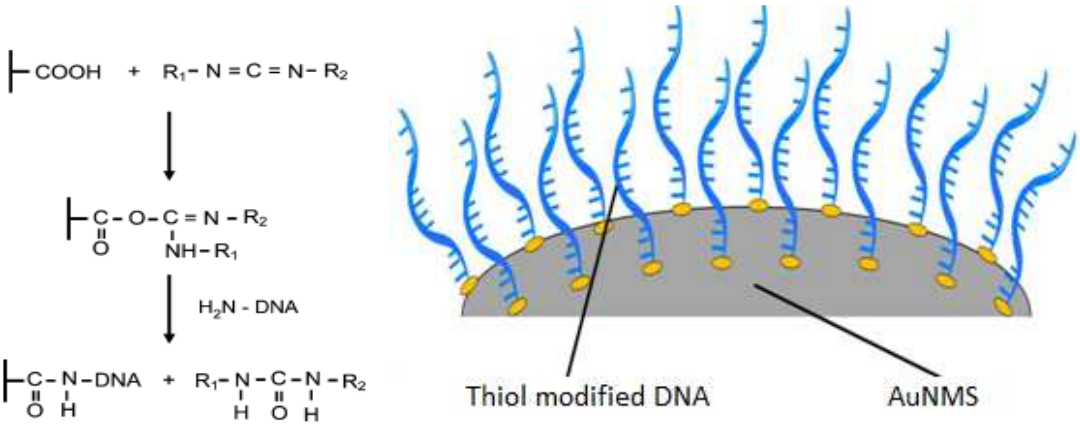

Figure 4. Schematic representation of DNA immobilization using EDC coupling and thiol modified AuNMs.

5.3 Detection techniques for Halal authentication

Specific target detection can be optically done by using fluorescence, surface plasmon resonance (SPR), chemiluminescence, colorimetry, interferometry, or surface-enhanced Raman scattering (SERS) spectroscopy. Electrochemical transducers have often been used for detecting biomolecular hybridization. There are numerous labeled electrochemical DNA sensors where the tag can be an enzyme, ferrocene, an interactive electroactive substance (a groove binder, such as Hoechst 33258, or an intercalator), or nanoparticles. Other label-free electrochemical DNA biosensors also have been reported. A Quartz Crystal Microbalance Sensors is a mass-sensitive sensor capable of measuring very small mass changes. It consists of a thin quartz disc sandwiched between a pair of electrodes. Quartz is a piezoelectric material that deforms when an electric field is applied across the electrode. The quartz crystal has a resonant frequency dependent on the total oscillating mass. Recently, Microcantilever detection have been imitated for detection biomolecular interactions. It is based on a response due to either surface stress variation or mass loading. Interaction between an immobilized ligand (e.g., a DNA probe) and an analyte (e.g., a DNA target) with ultimate change of the surface stress of the cantilever.

6. Nanomaterials for Halal food authenticaion

6.1 Gold nanomaterials

Gold nanomaterials (Au NMs) offer unique optical properties along with highly resonant particle plasmons. They can be synthesized at large size range (1-100 nm) and shape (1:1 - 1:5 aspect ratio) (Chithrani et al., 2006). Simple conjugation and upholding capability with different biomolecule offer Au NMs as ideal transducers (Cao et al., 2011; Taton et al., 2000; Zeng et al., 2011) for Halal authentication platform. Au NMs tailored probe for specific authentication with increase sensitivity may achieved by utilizing different dimensional gold nanostructures coupled with carriers probes and signalling molecules in microarray format (Storhoff et al., 2004). The key component of the Au NMs in probe hybridization detection is the surface plasmon absorption on distance-dependent surface (Wang et al., 2009). Effective hybridization of the specific target molecule causes the modification the dispersion with colour change (Figure 5) (Tan et al., 2011). The result of this phenomenon can be analysed by spotting the solution on a silica support or by using UV-vis spectroscopy (Elghanian et al., 1997; Li et al., 2004).

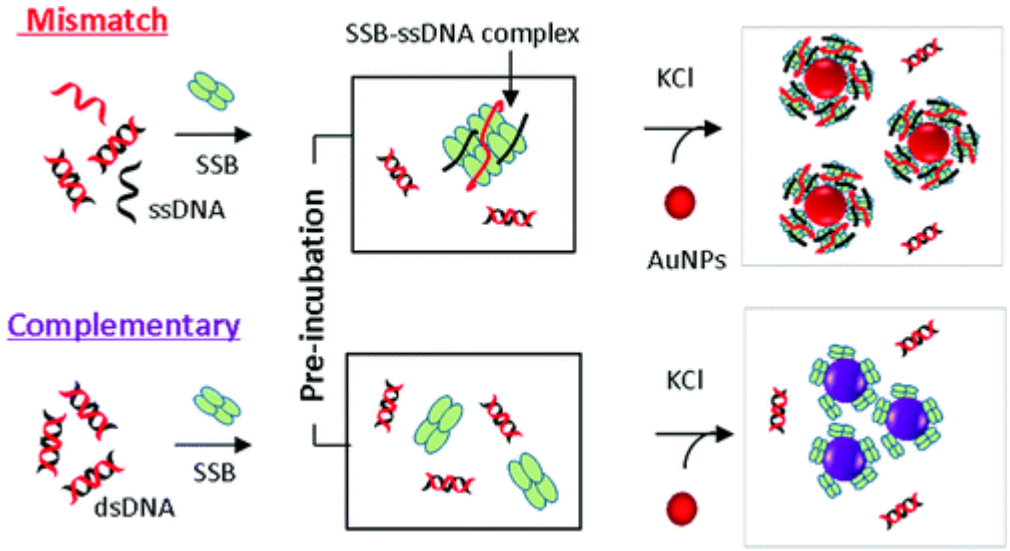

Figure 5. DNA detection principle based on the inverse relationship between sequence-dependent DNA hybridization based on SSB−ssDNA complex and Au NMs and change of the colour. Adapted from ref (Tan et al., 2011).

6.2 Silica nanomaterial

Silica nanomaterial with exclusive geometric properties in conjugation with various hybrid nanomaterials may offer a highly stable nano-platform with increased sensitivity. For example, dye-doped fluorescent silica nanomaterial may facilitate increase signal amplification (Wang et al., 2006) and magnetic silica nanoparticles assist molecular loading and transportation (Santra et al., 2001a; Trewyn et al., 2007). Silica surface provides a comprehensive bio tools for surface immobilization of DNA molecule for specific target detection (Figure 4) (Zhou et al., 2010). Furthermore, sandwich silica based DNA detection assay composed of a capture DNA immobilized on a glass surface; a probe sequence attached to TMR-doped silica nanoparticles; and the unlabelled target sequence complementary to both the capture sequence and probe sequence (Figure 6) (Zhao et al., 2003). Today's, there is an enrich silica surface modification database. Silica matrix shielding generate better photostability (Santra et al., 2001b). Silica nanoparticles embedded fluorophores labelling prevent atmospheric oxygen degradation and provide persistent fluorescence quantification. Thus probe modification with silica fluorophores

enclosed by silica network will facilitate ultrasensitive detection with enhanced signal amplification for halal authentication (Zhao et al., 2003).

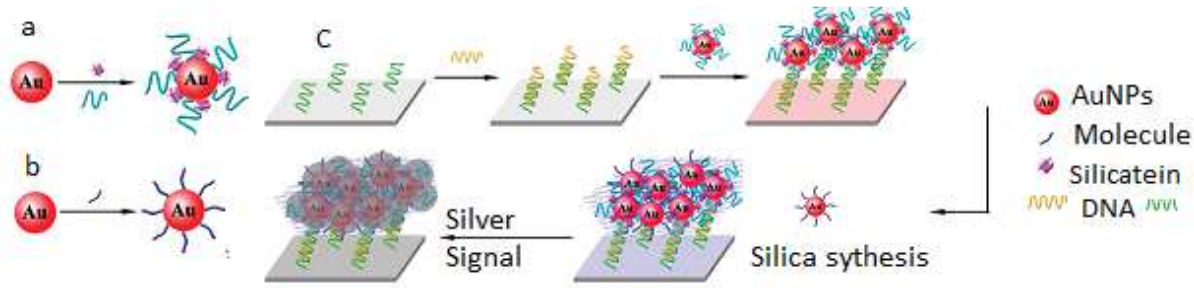

Figure 6. Silica as bio-tools for AuNPs assisted DNA detection based on AuNP probe through the visual readout of silver signal. Adapted from ref (Zhou et al., 2010).

6.3 Carbon nanomaterials

Carbon nanotubes (CNTs) are important nanomaterials with cylindrical structure with superior optical and mechanical properties for DNA detection (Prato et al., 2007). They are basically seamless rolled up graphene sheets of carbon and divided into single-walled nanotubes (SWNTs) and multiwalled nanotubes (MWNTs). The effective mechanism of specific DNA target detection is based on a non covalent attachment with the side wall of SWNTs by π-π interaction. Fluorescence signal amplification properties of SWNTs with specific DNA target in aqueous medium (Jeng et al., 2006) made them very suitable for electrochemical detection (Wang et al., 2003a). Hybridization of biocatalyzed SWNTs with nanowire-based detection methods offer a highly sensitive and specific platform for the fabrication of simple and effective conductometric DNA detection platform (Figure 7) (Weizmann et al., 2011). Recent nanotubes based DNA sensors open up a wide scale array ability with increase sensitivity (Tang et al., 2006). Furthermore, a simple halal authentication platform using a fluorescent sensing can be achieved by utilizing SWNTs based on the noncovalent assembly and dye-labelled single-stranded DNA (ssDNA) (Yang et al., 2008).

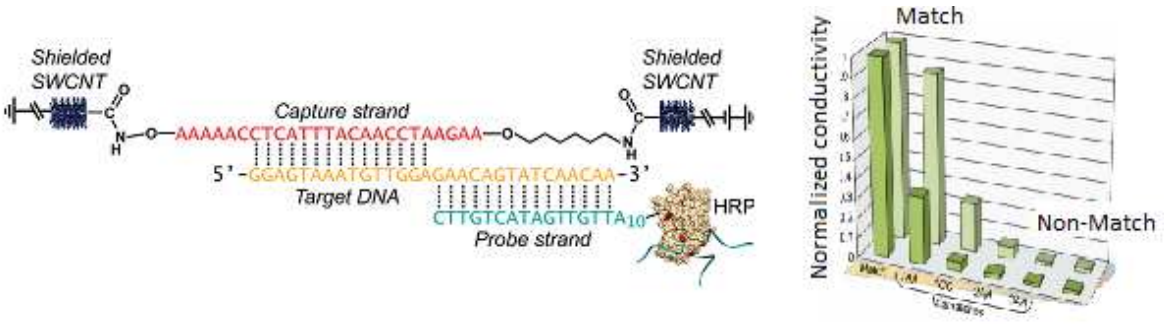

Figure 7. Schematic of SWNTs assembly and signalling bimolecular interactions with specific DNA hybridization detection. Adapted from ref (Weizmann et al., 2011).

6.4 Quantum Dots

Quantum Dots (QDs) are inorganic semi-conductor nanocrystals with size-dependent stable luminescence properties with high quantum yields, broad absorbance bands, but narrow emission spectra and high photochemical stability against photo-bleaching (Ho et al., 2005). Halal authentication platform incorporating QDs for food species detection can be achieved without separation-free format of different hybridization steps (Zhang et al., 2005). Furthermore, QDs have distinct photophysical properties for DNA analysis (Wang et al., 2009) and incorporation with probe may facilitate for an increase in its sensitivity. Recent modification of DNA probes with controlled microbeads embedded different sized QDs facilitated multiplexing detection technique. Three encoding nanoparticles (zinc sulfide, cadmium sulfide, and lead sulfide) have been used for a sandwich hybridization assay to differentiate the signals of three DNA targets (Figure. 8) (Wang et al., 2003b).

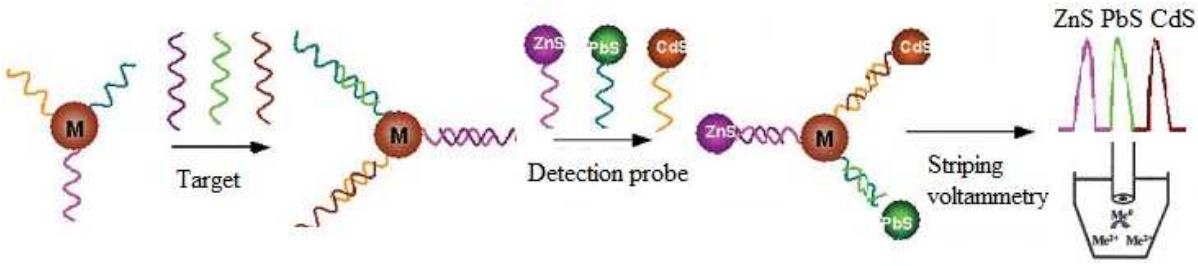

Figure 8. Scheme of QDS Multitarget electrochemical detection of DNA using QD labels. Adapted from ref (Wang et al., 2003b).

7. SERS as a potent food authentication tool

In the last three decades developemnt of the biomolecular signal detection using the advent surface-enhanced Raman scattering (SERS) with Raman spectroscopy bring straightforward laboratory tools even with fieldportable devices. SERS provide opportunity for both labeled and label-free identifications of small target analytes with wider applications ranging from biomarker detection for Halal authetication to homeland security (Figure 9). It mimics a future halal food authetication platform with higher sensitive exploiting nanopartilce conjugated materials with "fingerprinting" ability (Figure 10) (Krpetić et al., 2012). Extrinsic SERS mechanism of molecular recognitation offer benefits over conventional fluorescence-based assays. Raman peaks with 10–100 times narrower spectral widths than fluorescence labels and minimizing the overlap between different labels showed it increased multiplexing potentiality. Laser excitation and strong signaling capability of SERS active moleule provide multiple labelling capability using a single source. Furthermore, SERS labels are not susceptible to traditional photobleaching. It eliminated expensive reagents or time-consuming sample preparation steps associated with other techniques such as polymerase chain reaction (PCR) or immunoassays.

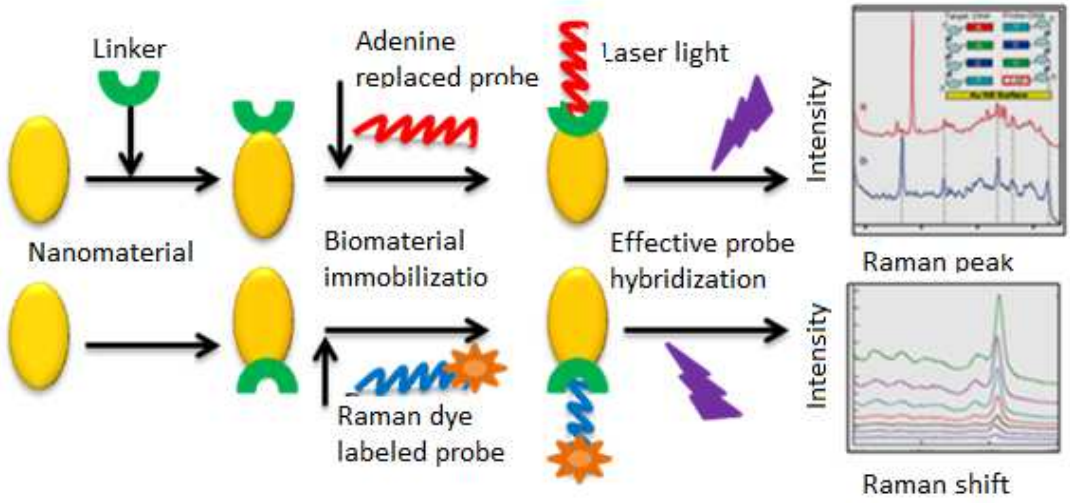

Figure 9. Functionalization of SERS active nanomaterials and dection of specific target hybridization.

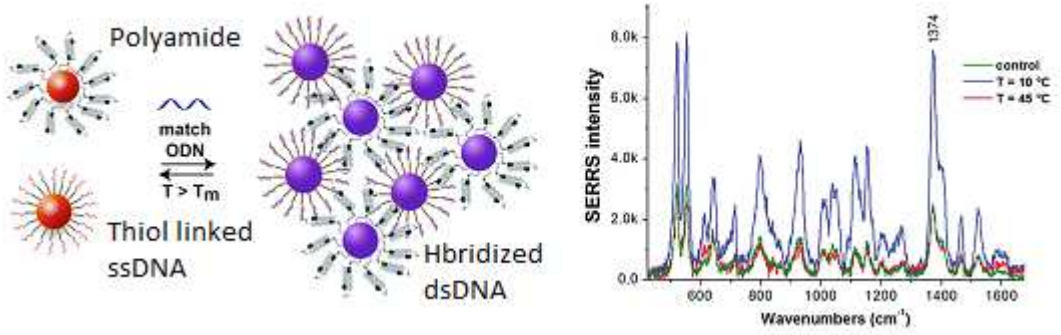

Figure 10. Schemetic representation of DNA detection where ssDNA-functionalized AuNPs and their subsequent aggregation were measured by SERS. Adapted from ref (Krpetić et al., 2012)

8. Conclusion and future prospective

The authentication of food is a vital part to ensure quality foods in compliance with fair prices and religions. For food authentication, DNA based method gains much interests due to its stability as compared to lipid-based and protein-based under different food processing conditions. Along with PCR, nanotechnology came forward with utilization of optical, electrochemical screening approaches for halal authentication based on bio-recognition events on solid devices and in solutions with better accuracy and sensitivity. Nanomaterials provides an easy and simple analytical sensor with high sensivity for halal authentication. Intense development of the biomarker probe, as well as optimization of detection protocol for halal authentication are on going. Amongst NM used includes nanogold, nanosilica, nanocarbon, quantum dots, and the emerging surface-enhanced resonance spectroscopy, SERS. The surface modified cost effective nanomaterials-based sensor has potential to be developed from laboratory tools to portable devices.

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