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1   **Title:** Dispersive and FT-Raman spectroscopic methods in Food Analysis

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22   Raman spectroscopy is a powerful technique for molecular analysis of food samples. A

23   fingerprint spectrum can be obtained for a target molecule by using Raman technology, as

24   specific signals are obtained for chemical bonds in the target. In this way, food components,

25   additives, process and changes during shelf life, adulterations and numerous contaminants

26   such as microorganisms, chemicals and toxins, can also be determined with or without the

27   help of chemometric methods. The studies included in this review show that Raman

28   spectroscopy has great potential for food analyses. In this review, we aimed to bring together

29   Raman studies on components, contaminants, raw materials, and adulterations of various

30   food, and attempted to prepare a database of Raman bands obtained from food samples.

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Introduction

Customers have recently become more concerned about being informed on food quality and, thus the need for food quality determination methods has increased. Therefore, all steps in food production such as composition or quality of the products, their origin and how they have been handled, processed and stored have gained importance. Various types of methods, including microbial methods, sensory analysis, biochemical and physicochemical methods are used in food analysis. Chromatographic methods such as high-performance liquid chromatography (HPLC) and gas chromatography (GC) have become very popular for separation and identification of food components due to their high reproducibility and low detection limits.[1] Deoxyribonucleic acid (DNA) based methods, such as Polymerase Chain Reaction (PCR) techniques, and immunological based methods, such as Enzyme-Linked Immunosorbent Assay, are also used for detection of specific targets in food samples. Although these are common methods being used, they cannot meet the demand for *in situ*, rapid and multiple analysis. Spectrophotometric methods, on the other hand, has a great advantage over them as it successfully meets those requirements. Spectroscopic methods which are used to determine different properties of food components is a rapid and easy method.[2] The spectroscopic methods used for food analysis include Ultra Violet-Visible Spectroscopy (UV-Vis spectroscopy), Fluorescence Spectroscopy, Raman Spectroscopy and Infrared Spectroscopy (IR), Circular Dichroism (CD), X-ray Spectroscopy, Nuclear Magnetic Resonance, Electron Spin Resonance, Dielectric Spectroscopy, and Photoacoustic Spectroscopy.

Raman spectroscopy detects chemical and organic molecule types and their physical structures by making use of bonds.[2] Photons are scattered when an intense monochromatic light source -especially a laser beam- irradiates a sample, and as a result of this application,

62   the largest fraction of the scattered light is found to have the same wavelength as the laser

63   light. This elastic scattering is known as Rayleigh scattering. Far fewer inelastic collisions

64   occur between the sample and the incident photons. As a result, the wavelengths of scattered

65   photons change, which is referred to as Raman scattering (Fig.1). If a molecule gains energy

66   during Raman scattering, the scattered photons will shift to longer wavelength and give

67   Stokes lines; however, if it loses energy, they may shift to shorter wavelengths and give anti-

68   Stokes lines, as seen in Fig 1.[3] The quantity of normal vibrations, masses and geometric

69   arrangements of the atoms in the molecule, as well as the strengths of the chemical bonds

70   between the atoms, form the vibrational spectrum or *fingerprint* of each molecule. The term

71   fingerprint is justified by the fact that no two samples or compounds have the same spectrum

72   in terms of frequency and intensity of peaks and shoulders.[4] Molecules have a large number

73   of vibrational states, but not all molecules are able to have a Raman spectrum. Being Raman

74   active is the basic requirement for a molecule to have a Raman spectrum. Raman

75   spectroscopy can examine molecular vibrations that cause change in their polarizability.[5] The

76   symmetry of a molecule is also an important requirement for Raman spectra, since symmetric

77   stretches are more intense in Raman spectra than in Infrared spectra. Functional groups such

78   as C-X (X=F, Cl, Br or I), $C-NO_2$, C-S, S-S, C=C, C≡C, C≡N, etc., show greater

79   polarizability changes and give strong Raman signals.[5]

80   A Raman spectrum consists of scattering intensity (photons per second) plotted vs.

81   wavelength (nanometres) or Raman shift (in reciprocal centimetres). Each band in a Raman

82   spectrum corresponds to a Raman shift occuring due to the incident light energy.[6] These

83   bands correspond to specific bands of chemical bonds and/or functional groups of the

84   molecule. By using these specific bands, the fingerprint of a molecule can be obtained with

85   Raman spectroscopy. In addition, quantitative analyses can also be performed by using

86   Raman spectroscopy since the intensity of the band is linearly proportional to the

87   concentration of an analyte.[3]

88   Raman spectroscopy has great potential for biochemical analysis. Major advantages of

89   this technique are its ability to provide information about concentration, structure, and

90   interaction of biochemical molecules within intact cells and tissues non-destructively. In

91   addition, it doesn't require homogenization, extraction, the use of dyes or any other labelling

92   agent,[7] or any pre-treatment of samples; it only requires small portions of samples. Raman

93   spectroscopy can analyse samples in both liquid and solid phases at ambient temperature and

94   pressure.[8] Besides, Raman spectroscopy is a potential tool for the assessment of food quality

95   systems during handling, processing and storage.[9]

96   In this review, we will discuss applications of Raman spectroscopy in food analysis

97   (Fig. 2). Conventional analysis methods will be taken into consideration under the headings

98   related to each basic food sample. These headings are listed as Raman Spectroscopy for

99   detection of food components, microorganisms and chemicals in food, food additives, raw

100 materials and food adulterations; and relevant studies are presented under each of them. In

101 addition, vitamins and minerals will be also considered although they found little interest in

102 food analysis by Raman despite of their major role in nutrition and health. There are several

103 reviews in literature about usage of Raman Spectroscopy for food analysis focusing on

104 specific food groups or spesific components found in foods.[10-13] This review will provide a

105 general insight into the Raman analysis of major components and contaminants found in

106 foods including adulterations. Besides, Raman bands of the important compounds found in

107 food matrix will be presented in a database, which will be helpful for the user of the Raman

108 spectroscopy to analyze new spectra obtained from food samples. Although surface-enhanced

109 Raman Spectroscopy (SERS) is a commonly used method for improving the sensitivity of

110 Raman Spectroscopy, studies on SERS haven't been included in this review since it requires a

111   specific surface and a Raman active molecule in order to provide enhancement and to obtain

112   characteristic Raman signals.

113

Raman spectroscopy for the detection of food components

115   Composition of the food samples has great importance due to its substantial effect on quality,

116   nutritional and economic value, and its contribution to the properties of final product.

117   Environmental factors and applied processing factors could have both positive and negative

118   effects on food components. Therefore, monitoring these changes in every step of food

119   production process is of great importance. There are many ways to determine these changes in

120   food components, and for this purpose, there has been an increasing interest in the use of

121   Raman spectroscopy over the past few decades. In this section, an overview is given on the

122   use of Raman spectroscopy in quantitative and qualitative analysis of food components.

123   Specific Raman bands related to the articles investigated in this section were given in Table

124   1S, 2S, 3S and 4S for proteins, carbohydrates, lipids and vitamins, respectively.

125

Proteins

127   Raman spectroscopy enables researchers to obtain detailed information on structural

128   properties of proteins. Studies on food proteins have been conducted for several decades, and

129   they still maintain their importance since proteins are one of the major components of foods

130   and have important effects on properties of food. Proteins are large polypeptides consisting of

131   hundreds of amino acids; thus, a complex set of overlapping bands forms their Raman spectra.

132   Additionally, strong Raman scattering of aromatic amino acids and polypeptide chains also

133   contribute to the existance of characteristic bands observed in the Raman spectra.[14]

134   Raman spectroscopy has been used in food protein studies on various topics, but in

135   particular, investigation of the secondary structure of proteins has been the focus of them. In

136   these studies, amide bands-especially the amide I (1645–1685 cm^{-1}) and amide III (1200–

137   1350 cm^{-1}) bands have proven to be the most useful bands to obtain data on the secondary

138   structures of proteins, which are composed of α-helices, β-sheets, turns and random coil

139   structures. Characteristic Raman bands of various amino acid residues have also been used to

140   acquire information about the microenvironment and conformational changes of the proteins.

141   For instance, phenylalanine residue has been generally used as an internal standard in most of

142   the Raman spectroscopic studies[15-17] since it is reported to be insensitive to conformation or

143   microenvironment.[18] Chi et al. used the advantages of UV-resonance Raman spectroscopy

144   (UV-RR spectroscopy), such as its ability to selectively examine the secondary structures of

145   dilute protein and peptide solutions.[19] Chemometric methods were employed to determine the

146   average amide band resonance Raman spectra of the α-helix, β-sheet, and unordered

147   secondary structures of a number of proteins. Similarly, Huang, Balakrishnan, and Spiro used

148   deep-UV-RR spectroscopy to investigate the secondary structures of proteins.[20] Resonance-

149   enhanced amide bands and aromatic side chain bands of proteins with varied secondary

150   structure contents were analysed with least-squares fitting method to establish quantitative

151   signatures of secondary structure.

152   Several reactions occuring in the food matrix due to application of different processing

153   techniques could be monitored by Raman spectroscopy. Nonaka, Li-Chan, and Nakai studied

154   thermal-induced gelation process of whey proteins. Different time and temperature parameters

155   were applied to α-lactoglobulin and β-lactoglobulin proteins, and changes in their Raman

156   spectra were followed.[21] In another study, Raman spectroscopy was used to investigate the

157   interaction of lysozyme, α-lactoglobulin and β-lactoglobulin before and after the completion

158   of gelation process.[22] Rheological changes and the interactions of egg albumen and whey

159   protein during the gelation process were tracked with FT-Raman spectroscopy using

160   phenylalanine (1004 cm^{-1}) as an internal standard. Differences in the gel structures were

161   evaluated by monitoring CH (1350 cm^{-1}) and CH$_2$ (1450 cm^{-1}) bending vibrations. As a result,

162   an increment was observed for the Raman intensity of β-sheet structures in the amide III

163   region, while the intensities decreased for helical structures.[17] Sánchez-González et al. used

164   FT-Raman to examine the structural changes in proteins and water during gelation of fish

165   surimi. Amide bands and amino acid residue bands were monitored to detect the changes.[23]

166   The changes in chemical structures occuring due to heat treated gelatinization of miyofibrillar

167   proteins contribute to the quality of meat products and to improve their production techniques.

168   Hence, conformational changes in peptid structures of meat, which is highy rich in protein,

169   were tracked by using Raman spectroscopy. It was found that owing to the impact of heat,

170   changes in amide I (1600-1700 cm^{-1}) and amide III (1200-1300 cm^{-1}) regions reduces the α-

171   heliks content in protein structure, while it increases β-sheets, β-turns and random coil

172   content.[24] In another study, whether endpoint temperature (EPT) was reached for cooked meat

173   and meat products was checked by using Raman Spectroscopy with chemometric analysis. It

174   was found that seconder structure of meat proteins were changed with heat treatment as in the

175   previous study.[25] Lim et. al., studied gelation of phenol extracted protein fractions from non-

176   acclimated (NA) and cold-acclimated (CA) winter rye leaf tissue after repeated freeze–thaw

177   treatments. Changes in the protein secondary structure caused by the freeze-thaw cycles were

178   monitored by using Raman microscopy. Gelling and non-gelling components as well as

179   protein extracts were individually analyzed with Raman measurements. Similarity between

180   NA and CA samples was explained with their similar structural conformations, which were

181   stabilized by similar protein-protein interactions, while dissimilarities were mainly assigned to

182   the covalent bonds altered by freeze-thaw treatments.[26] Lactate dehydrogenase was chosen as

183   a model protein to evaluate the potential of Raman spectroscopy for discriminating native like

184   and non-native states of protein in freeze-dried formulations. PCA and PLS–LDA methods

185   were applied to collected Raman data for discrimination studies. Different prediction models

186   were developed using different spectral regions and their combinations. C-N stretch, NH_3

187   deformation, amide III, and mainly $C-H_n$ non-stretching with possible participations of C-N

188   and C-C stretching were considered to have the maximum contribution to the success of

189   discrimination.[27]

190   Deamidation of proteins is another process which can be easily followed by using

191   Raman spectroscopy. Wong et al. used soy and whey protein isolates and spray-dried egg

192   white powder to analyze the extent of deamidation in food proteins. Conformational changes

193   of the protein structures were examined using Raman spectroscopy. Characteristic band,

194   which was assigned to the stretching of the C=O bond of glutamate or aspartate, was used as

195   the marker band for deamidation.[28] In another work, the enzymatic hydrolysis of wheat gluten

196   substrates, which were acid-deamidated by using three different acids were determined with

197   Raman spectroscopy. The same degree of deamidation with the same heat treatment

198   conditions was applied to all substrates. Raman spectroscopic analyses of microenvironments

199   belonging to Cys, Trp, Tyr and His amino acids showed a positive relation with their

200   susceptibilities to enzymatic hydrolysis.[16]

201   Kang et al. used Raman spectroscopy to evaluate the effects of salt content and also

202   chopping and beating processes on the structural components of pork frankfurters. In the case

203   of increased salt content, a decrease was observed for C-H stretching, CH_2 and CH_3 bending

204   vibrations, while no changes were witnessed for secondary structures, namely tryptophan,

205   tyrosine residues, β-sheet and α-helix. Beating process was resulted with an increase in β-

206   sheet, a decrease in α-helix content and a decrease in C-H stretching, CH_2 and CH_3 bending

207   vibrations. The adequacy of Raman spectroscopy as the experimental technique to follow the

208   changes (appearing and disappearing of compounds) in composition during the beating

209   process was demonstrated in this study.[29]

210   The interactions of proteins with other food components are another topic of interest

211 commonly dealt with in using studies Raman spectroscopy. Shao et al, for instance, used

212 Raman Spectroscopy to examine the emulsion created by adding lipid to meat. They followed

213 the changes occuring in protein structures due to addition of different lipids to meat and heat

214 treatment. They found that there wasn't a considerable change in the secondary structures of

215 proteins in emulsion spectra obtained by mixing three different kinds of lipids without any

216 heat treatment. With the application of heat treatment, however, it was seen that changes

217 occured in the bands (1153 cm^{-1}) demonstrating amide I (1654 cm^{-1}), amide II (1517 cm^{-1}),

218 amide III (1300 cm^{-1}) and C-N stretching vibration, and that formation of β-sheet increased.

219 In this way, the researchers put forward the idea that with Raman spectroscopy,

220 protein/lipid/water interactions could be examined and information could be obtained

221 directly.[30] Meng et al., however, examined the protein-lipid interaction with Raman

222 microscopy by using bovine serum albuimn/oil. Different spectra were obtained by extracting

223 the spectrum of mineral or corn oil from that of the bovine serum albumine (BSA)/oil

224 interface in order to determine the contributions of different functional groups to the protein-

225 lipid interactions.[31] In the study of Sivam et. al., Raman and FT-IR spectroscopy were used as

226 complementary methods to explore the conformational changes in wheat proteins and

227 polysaccharides due to their interactions with fruit polyphenols and pectin. Amide bands, in

228 particular, were examined to comprehend the interactions between additives and gluten

229 proteins by following changes in the secondary structures of the proteins.[32] In the study of

230 Ferrer et. al., gluten protein was chemically modified with an emulsifier, namely sodium

231 stearoyl lactylate (SSL), and the effect of the modification on the secondary and tertiary

232 structures of this protein was analysed with FT-Raman spectroscopy. A significant increase

233 was observed in the intensity of amide I band, which is attributed to a more ordered structure.

234 Conformational variations of disulfide bounds and the variations of the intensity rate of the

235   tyrosine doublet bands, tryptophan and C-H stretching band were also explained by formation

236   of a more ordered structure.[15] In the subsequent study of the same group, Gomez et. al.

237   reported a more detailed research investigating the conformational changes in the presence of

238   another emulsifier, namely diacetyl tartaric acid esters of monoglycerides: DATEM. A

239   comparison was also made on the differences in the gluten structures occurring in the

240   presence of DATEM and SSL, respectively. Differences on Raman spectra were mainly

241   assigned to the distinct chemical structures of these emulsifiers which specify their type of

242   interactions with gluten proteins.[33] Perisic et. al. used the combinations of vibrational

243   spectroscopic techniques, namely NIR spectroscopy and FT-IR, NIR and Raman

244   microspectroscopy to study the effects of different salts on the hydration properties of

245   structural proteins. Interactions between salt cations and aromatic amino acid residues were

246   investigated, and their effect on the final structure of proteins was emphasized. Effect of salt

247   concentration on the protein structures were mainly monitored with tyrosine bands which

248   were in a positive correlation with hydrogenated N-H groups.[34]

249

250   **Carbohydrates**

251   Structural characterization of carbohydrates is of great importance since they form the widest

252   class of organic compounds. Mono-, di-, oligo- and polysaccharides show characteristic

253   Raman bands by which carbohydrates can be easily determined and quantified. Presence of

254   large number of atoms in the repeat unit and absence of a well-defined entity increased the

255   importance of accurate assignement of vibrational modes in the structural analysis of

256   carbohydrates by using Raman spectroscopy.[35] For instance, the amylose contents of corn and

257   cassava starch samples were quantified using FT-Raman spectroscopy coupled with PCA and

258   PLS regression methods. Characteristic band at 480 cm^{-1} was assigned to the ring vibration of

259   starches and used to identify the presence of starch and to distinguish between corn and

260   cassava starch samples.[36] Delfino et al. quantified the glucose contents in commercial sports

261   drinks by using micro-Raman and interval Partial Least Square regression (iPLS). Fingerprint

262   bands of glucose, fructose and sucrose were obtained in the spectral region between 600

263   and1600 cm^{-1}.[37] In a recent study reported by our research group, Ilaslan et. al. used Raman

264   spectroscopy to quantify glucose, fructose and sucrose contents of commercial soft drinks.

265   Additives in the content of soft drinks were also characterized by their bands, which were

266   assigned to the presence of aroma compounds and citric acid in the composition. The

267   calibration curves were obtained for each component by applying PLS regression on Raman

268   data, and validation studies were carried out using HPLC.[38]

269   Raman spectroscopy was also used for the detailed investigation of structural

270   components of the food samples. In the study of Roman et al., the components of wild carrot

271   root, such as starch, pectin, cellulose, lignin, and even bioactive polyacetylenes were

272   measured in situ and without any sample preparation. They also showed tissue-specific

273   accumulations of the components using a Raman mapping technique.[39] In a similar study,

274   components of wheat and barley grain were investigated using Raman microscopy. The

275   Raman spectra of the most important substances such as proteins, carbohydrates

276   (arabinoxylan, β-glucan and starch) and phytic acid were included in the compositions of

277   barley, and wheat cells were measured. Wheat proteins were monitored by using the

278   characteristic bands of gluten located around 1449 and 1659 cm^{-1}, which was attributed to the

279   CH$_2$ bending mode of amino acids and C=O stretching mode of amides, respectively.

280   Polysaccharides, namely arabinoxylan, β-glucan and starch gave similar Raman spectra.

281   Distinct bands at 1095 and 1120 cm^{-1} assigned to the COC stretching vibrations of glycosidic

282   bonds showed the most evident similarity between these spectra. Starch was separated from

283   the other polysaccharides by its characteristic bands at 480 and 901 cm^{-1} (skeletal vibrations

284   of the glucopyranose ring), and phytic acid gave relatively weak Raman scattering with a

285 characteristic band at 3420 cm$^{-1,}$ (stretching of OH group). Raman imaging was also

286 performed to analyze the distribution of these components in the cereal grain structure.[40]

287   Application of Raman spectroscopy makes it possible to determine the sources of

288 carbohydrates and extract minor differences between very similar structures. Scudiero and

289 Morris used Raman spectroscopy to identify the differences between soft and hard wheat flour

290 samples. Relative intensity ratios of the bands between 400-600 cm^{-1} and 1020-1650 cm^{-1}

291 corresponding to the arabino-to-xylan substitution and phenolic acid contents were used to

292 differentiate the samples.[41] Wellner et al. compared the composition and physical structure of

293 starch granules found in wild type and mutant maize kernels by using a Raman imaging

294 technique.[42] Similar characteristic bands of carbohydrates and protein structures, specifically

295 amide I bands were observed for both wild type and mutant samples. However, differences

296 originating from the variations in the ratio of branched residues to linear residues were

297 monitored by following the characteristic band at 942 cm^{-1}, which was reported as being

298 sensitive to the level of branching in starch polysaccharide. Another characteristic band at 865

299 cm^{-1} was used to monitor the crystalline structure of starch granules.[43] Compositional and

300 structural properties of β-glucan in barley and oat samples were investigated with FT-Raman

301 spectroscopy. PCA and PLS regression were used for multivariate data analysis of collected

302 Raman data, especially in the spectral region between 800 and 1800 cm^{-1}. PLS regression

303 prediction models successfully determining the β-glucan and starch contents of the samples

304 were created. Clusters of cellulose, curdlan and cellulose-curdlan blends were located in the

305 PCA score plot depending on the variation in their β-glucan structure.[44]

306   The effects of food processing on carbohydrates, one of which is starch modification,

307 have also been analysed with Raman spectroscopy. Chong et al. determined the degree of

308 maleate substitution in maleinated starches depending on the emergence of new bands, which

309 were likely due to nominal C=O stretch, C=C stretch, and O-H stretch vibrational modes.[45]

310   Another modification of starch was carried out with octenyl succinate. This modification

311   treatment was monitored using Raman microscopy entegrated with AFM.[46] The use of Raman

312   spectroscopy for quality control of modified starches in the food industry was demonstrated

313   by Dupuy and Laureyns. They identified the modified starches according to their origin and

314   type of modification. Although an overall similarity was observed for different starch

315   samples, disappearance of the doublet at 600 cm^{-1} was observed for pregelatinized samples.

316   Similarly, waxy samples were monitored by their characteristic bands at 480, 870, 950 and

317   1468 cm^{-1}, which were assigned to skeletal mode, the CH and CH_2 deformation, the skeletal

318   mode involving α (1–4) linkage and the CH_2 deformation, respectively. They also compared

319   the efficiency of the chemometric methods PCA and PLS in order to group the samples

320   according to the applied modification type and draw the conclusion that PLS is more effective

321   than PCA.[47] Passauer et al. studied the degrees of substitution (DS) of starch phosphates by

322   using the characteristic band of C-O-P stretching vibration at about 975 cm^{-1}.[48] Volkert et al.

323   also determined the DS values of different substituted starch acetates by using a combination

324   of FT-Raman spectroscopy and chemometrics. They found the best congruence between

325   determined and calculated DS values by calculating the first derivatives of the Raman

326   spectra.[49] In another study, DS values for cationic quaternary ammonium starches were

327   determined using the characteristic band of trimethyl ammonium substituent about 761 cm^{-1}.[50]

328   Similarly, the DS values for carboxymethylated non-starch polysaccharides including

329   cellulose, guar gum, locust bean gum and xanthan gum were determined with Raman

330   spectroscopy and a colorimetric method. The characteristic band at 1607 cm^{-1} was chosen to

331   be the marker of carboxymethylation which originates from C=O carbonyl stretching

332   vibration. The intensity ratios of the marker bands to that of an internal standard band

333   corresponding to the skeletal configuration and linkages (850–950 cm^{-1}) were used to

334   establish a calibration between spectroscopic and colorimetric DS values.[51]

335   In another study, the technical starch hydrolysis process was monitored with FT-

336   Raman.[52] Gelatinization, liquefaction, saccharification and retrogradation processes were

337   evaluated within the context of the relevant study. The intensity of the bands at 1633 and 3213

338   cm^{-1} increased during the gelatinization process, while the others decreased. Liquefaction was

339   characterized by the disappearance of the bands at 735 cm^{-1} and 480 cm^{-1}. Changes in

340   saccharification at bands in 910–935 cm^{-1} region and at 1127 cm^{-1} were also monitored. [53, 54]

341   Mutungi et al. demonstrated the utility of the FT-Raman method for rapidly determining

342   starch crystallinity, which is important for food production and storage. In this method, a band

343   assigned to symmetric C(1)-O-C(5) stretching of the α-D-glucose ring was used as an internal

344   standard to normalize the spectra. As a result, a strong linear correlation was found between

345   crystallinity and the integrated area of the skeletal mode Raman band.[55] Similarly, in the study

346   of Islam and Langrish, Raman spectroscopy was used to investigate the formation of lactose

347   anomers and degree of lactose crystallization during spray drying. The characteristic bands in

348   the Raman spectra indicated the presence of different lactose anomeric and crystalline forms.

349   These bands at 1100 and 350 cm^{-1} were assigned to the stretching and bending vibrations of

350   the C-O-C grouping of α- and β-lactose structures. Spectral region between 1200 and 1500

351   cm^{-1} was used to characterize the presence of an amorphous polymorph in the lactose

352   samples.[56] In another study on crystallinity, Raman spectroscopy was used to determine the

353   viscoelastical properties of modified cellulose, which is a significant substance in food

354   industry. Akinosho et. al. investigated the effect of methyl and hydroxypropyl groups on gel

355   properties of hydroxypropyl methylcellulose (HPMC). Subsequent to the analysis of collected

356   Raman data, usability of the hydroxypropyl groups as an indicator of the crystalline structure

357   of HPMC was reported. Crystallinity was also monitored by following the significant

358   broadening, which is generally assigned to the decrease in crystallinity in the spectral region

359   between 1540–1660 cm^{-1}.[57]

360   Kizil and Irudayaraj evaluated the potential of Raman spectroscopy to follow the

361   chemical changes induced by the application of gamma-irradiation to food samples. Fructose

362   and honey samples were analysed using FT-Raman spectroscopy and canonical discriminant

363   analysis was applied to the collected data. Monitoring the CH stretch region between 2800

364   and 3000 cm^{-1}, they classified honey samples according to applied irradiation dose. Using

365   spectral regions below 700 cm^{-1} and between 800 and 1500 cm^{-1}, changes in the ring and

366   conformational structure of the fructose induced by irradiation were identified.[58]

367   The mechanism of thermal radical generation in cereal starches with different amylose

368   contents was analysed by using a Raman microspectrometer. Effects of high temperature on

369   the structure of polysaccharide molecules were tracked from the collected Raman spectra.

370   Due to the decomposition of polysaccharide chains by the cleavages of the glycosidic bonds,

371   the highest amount of decrease was observed for the bands at υ_a (1150 cm^{-1}) and υ_s (944

372   cm^{-1}) of C-O-C.[59] Different from the previous one, in this study, how freezing treatment

373   affects the structure of wheat bread dough was examined with Raman spectroscopy. The

374   distribution of ice free water, starch, gluten and yeast in the frozen dough in the structure was

375   determined by examining the Raman bands of each of these components, and the

376   microstructure of the dough was determined by making use of images. In this way,

377   researchers stated that the causes of the decrease in quality can be found in the frozen baked

378   goods.[60]

379

380   **Lipids**

381   Lipids are one of the three major food components, but they have been reported as the most

382   complex molecular structures to be analysed. Raman spectroscopy has been widely used for

383   determining different properties of lipids. For instance, Sadeghijorabchi et al. put forward a

384   procedure that determines the total level of unsaturation in oils and fats by using FT-Raman

385   spectroscopy.[61] Similarly, Silveira et al. quantified unsaturated fats in fat-containing foods.

386   Raman spectra of edible oils, margarine, mayonnaise, hydrogenated fat, and butter were

387   obtained with a near-infrared Raman spectrometer by making use of this non-destructive

388   quantification method. Spectral regions of 1750, 1660, 1440, 1300, and 1260 cm^{-1} were used

389   to establish a correlation between Raman intensities and the total and unsaturated fat contents

390   of analyzed samples.[62] El-Abbasy et al. quantified the fat content in liquid homogenized milk

391   by using VIS-Raman spectroscopy. Protein and carbohydrate content of milk samples didn't

392   made a significant influence on the Raman intensities, so the variations were directly

393   attributed to the fat contents of the samples. Characteristic bands were mostly assigned to the

394   fatty acids and monitored at bands in 1650 cm^{-1} (C=C *cis* double bond stretching of

395   RHC=CHR), 1440 cm^{-1} (C–H scissoring of –CH_2), 1265 cm^{-1} (C–H bending at the *cis* double

396   bond in R–HC=CH–R), 1300 cm^{-1} (C–H twisting of the CH_2 group), and 1747 cm^{-1} (C=O

397   stretching of RC=OOR).[63] McGoverin et al. used Raman spectroscopy to quantify milk

398   powder constituents, namely protein and fat in skim and whole milk samples. The overlapped

399   bands seen in Raman spectra are considered to be caused by lactose, milk proteins and milk

400   fats. The characteristic band represented by lower wavenumber 1745 cm^{-1} C=O modes were

401   assigned to milk fat, while the phenylalanine ring breathing band at 1005 cm^{-1} was accepted

402   as the indicative of protein. A low broad peak above 3300 cm^{-1} was reported to be consistent

403   with N-H and O-H modes of protein and lactose.[64] A combination of Raman spectroscopy

404   with chemometric methods enabled researchers to establish predictive models for these

405   constituents by using abovementioned characteristic bands. This combination has also been

406   used to predict the abundance of fatty acids in clarified butterfat,[65] and to discriminate and

407   classify different oils and fats.[66-68] Marquardt et. al. used Raman spectroscopy to obtain

408   quantitative data on carotenoid, collagen and fat contents of the fish muscle samples. Fat

409   content was characterized by the bands at 657, 1440, 1301 (CH_2 in phase twist), 1267(C–H

410   symmetric rock (*cis*)), 1076 (C-C-C stretch) and 1064 cm^{-1} (C-C-C stretch). Carotenoids were

411   monitored at primary bands (1159 and 1518 cm^{-1}), and the intensity of the bands at 857

412   (proline) and 940 cm^{-1} (C-C stretch of peptide backbone) which were assigned to the

413   presence of collagen was found to be relatively weak.[7]

414   Lipid oxidation, one of the most important quality indicators in foods, has been

415   investigated with Raman spectroscopy. Muik et al. examined the chemical changes that

416   occurred during lipid oxidation in edible oils.[69] Kathirvel et al. monitored the progression of

417   lipid oxidation in mechanically separated turkey by monitoring the oxidative bleaching of ß-

418   carotene using Raman spectroscopy. Three characteristic Raman bands at 1008 cm^{-1} from the

419   C-CH$_3$ rocking, at 1160 cm^{-1} from the C-C stretching and at 1524 cm^{-1} from the C=C

420   stretching were observed for ß-carotene molecule, while the last one was used to monitor its

421   concentration.[70] Guzman et al. determined the oxidation status of olive oil through a

422   combination of low-resolution Raman spectroscopy and PLS analysis. In order to monitor

423   olive oil oxidation, characteristic Raman bands at 1267 cm^{-1}, 1302 cm^{-1}, 1442 cm^{-1} 1655

424   cm^{-1}, and 1747 cm^{-1} (corrseponding to symmetric rock double bond in *cis* =CH, in-phase

425   twist methylene, methylene scissoring mode of CH$_2$, *cis* double bond stretching (C=C), and

426   ester stretching (C=O), respectively) were detected in the region below 1800 cm^{-1}.[71] In

427   addition to these applications, it is also possible to show the effects of storage conditions on

428   lipids or lipid containing foods. Sanchez-Alonso et al. used FT-Raman spectroscopy to

429   monitor the lipid oxidation of hake fillets during frozen storage. C-C stretching vibration at

430   1658 cm^{-1} was reported as the only characteristic Raman band related to the lipid oxidation.[72]

431   A study was carried out using linoleic acid, which is a very important fatty acid in

432   human diet. In this study, linoleic acid was treated with high pressure. Linoleic acid's phase

433   transtion and conformational changes with high pressure were observed in real-time by using

434   Raman spectroscopy. Significant conformational changes were observed at 0.07-0.12 GPa and

435 0.31-0.53 GPa. With the increase in pressure, some Raman bands disappeared, while some of

436 them appeared. The researchers believe that knowledge about these chemical and physical

437 changes will make the major contribution to food preservation technology.[73] Another essential

438 oil produced out of *Lamiaceae* plant displaying different chemical profiles according to their

439 genomic properties has a biological activity of great importance. In the light of these

440 informations, chemical structures of the essential oils were determined using dispersive

441 Raman spectroscopy and FT-IR. Chemotyping was based on characteristic bands of thymol

442 (740 cm^{-1} ring vibration) and carvacrol (760 cm^{-1}), and the reasults were confirmed by using

443 GC.[74]

444   Researchers used Raman spectroscopy to follow the changes in carotenoid structure of

445 extra virgin olive oil with heat treatment, which was applied by using microvave and

446 conventional heating processes. It was shown that conventional heat treatment caused more

447 rapid degradation of caretoneid bands at 1008 cm^{-1} (C–CH_3 bend), 1150 cm^{-1} (C–C stretch),

448 and 1525 cm^{-1} (C=C stretch). In addition, the researchers found that high heat treatment

449 resulted in whole degradation of caratenoids and that application time plays a more important

450 role in the degradation compared to high temperature. They determined that heat treatment

451 with microwave during oil rafination affects the oil quality less than the conventional heat

452 treatment since the desired temperature was achieved by microwave more quickly than

453 conventional heating.[75]

454

455 **Vitamins**

456 A variety of analytical procedures have been used for vitamin analysis in food samples. Lack

457 of specify and matrix effect were reported as the main disadvantages of these procedures. On

458 the other hand, Raman spectroscopy has gained an increasing importance due to its high

459 precision and good signal-to-noise rate for vitamin analysis.[76]

460   Investigation of vitamins with Raman spectroscopy began in the 1970s. Main goals of

461   these early studies were to characterize the isomeric forms[77] and obtain the characteristic

462   Raman spectra of vitamins.[78] Rimai et al. acquired the Raman spectra of retinals (*trans*, 9-*cis*,

463   13-*cis*), retinols (*trans*, 13-*cis*), and *trans*-retinoic acid in octanol solution and reported the

464   possibility of characterizing the terminal group on vitamin A type molecules and isomers by

465   their characteristic bands at around 1580–1590 cm^{-1} and 1100–1400 cm^{-1}.[77] Similarly, Tsai and

466   Morris researched the effect of pH and other water soluble vitamins on Raman intensity of

467   Vitamin B12 by using cyanocobalamin as a model chemical. A strong Raman band at 1504

468   cm^{-1} corresponding to the ring stretching vibration of molecule was followed.[79] Also,

469   Cimpoiu et al. coupled high performance thin layer chromatography (HPTLC) with Raman

470   spectrometry in order to obtain a suitable method for identification of eight hydrophilic

471   vitamins, i.e., B1-thiamin, B2-riboflavin, B3-nicotinic acid, B5-panothenic acid, B6-

472   pyridoxine, B9-folic acid, B12-cyanocobalamin, and C-ascorbic acid in different samples. In

473   this study, a successful separation was achieved by HPTLC, and vitamins were easily

474   characterized by Raman spectroscopy.[80]

475   The use of Raman microscopy also made it possible to determine and localize

476   vitamins in biological samples. Kim and Carey used riboflavin to differentiate free vitamins

477   and vitamins bound to vitamin binding proteins at micro molar concentrations.[81] In another

478   study, Beattie et. al., used Raman spectroscopy to identify α-tocopherol, which is known to be

479   the predominant form of vitamin E in biological samples.[82]

480   Additionally, chemometric techniques were used in order to quantify vitamins in

481   powdered mixtures and solutions. Spectral regions between 2800-3000 cm^{-1} and 800-1750

482   cm^{-1} were used for the PLS models due to their high correlation with Vitamin C

483   concentrations. A detailed chemical assignment was given in the relevant study.[83]

484

485   # Raman spectroscopy for microorganism and virus detection

486   There are several analytical methods to determine the presence of microorganisms and

487   viruses. Although traditional microbiological plate count methods such as PCR, and

488   immunological and serological methods have been frequently used for this purpose, Raman

489   spectroscopy has gained increasing attention due to its abovementioned advantages such as

490   high sensitivity, reliability and non-destructiveness.[84] In addition to microorganisms that grow

491   in food, Hepatitis A and Norwalk viruses, Poliovirus, Astrovirus, Enteric adenovirus,

492   parvovirus and rotaviruses have also been found in foods as contaminants.[84, 85] Specific

493   Raman bands for microorganism and virus detection were given in Table 5S.

494

495   **Microorganisms**

496   Raman and its derivatives, such as UV-RR, FT-Raman, Micro-Raman and Confocal Raman

497   can be used to determine the presence of microorganisms. By carefully selecting which

498   Raman method to use, taking advantage of neural networks, and utilizing chemometric

499   methods to make qualitative distinctions between spectra; it is possible to identify and

500   differentiate microorganisms.[86, 87]

501   *Bacillus* and *Brevibacillus* species are spore-forming bacteria. *Bacillus* species, in

502   particular, is pathogenic and causes serious food poisoning incidences; they can also be used

503   as a biological weapon. Passage from the spore to the vegetative forms of these bacteria, and

504   determining the effects of manganese dipicolinate and calcium dipicolinate upon spore

505   formation, were monitored with micro-Raman spectroscopy.[88] In a study made on spore-

506   forming *Clostridium* cultures, single-cell spectra were collected using confocal Raman

507   microscopy. Although the morphological structures of the cells were similar, significant

508   spectral differences were observed between them and their contents depending on age and

509   spore production. As a result, chemical differences between the cells were easily identified by

510   Raman microscopy.[52]

511   In another study with confocal Raman microscopy, a group of pathogenic

512   microorganisms (*Enterococci* and *Staphylococci*) was classified. Raman measurements were

513   taken from different regions of a microcolony of each culture and processed with

514   chemometric methods. When dendrograms obtained with Hierarchical Cluster Analysis

515   (HCA) were analysed, two arms were observed, one of which belongs to *Enterococci* and the

516   other to *Staphylococci*.[89] Specific strains of *Staphylococcus* were identified with a micro-

517   Raman system. With this methodology, it was possible to determine chemotaxonomic

518   classification for a single cell and bulk cultures. HCA and Support Vector Machine (SVM)

519   were used as statistical methods. In one of the analyses, all of the bacteria were incubated

520   under the same conditions (medium type, incubation temperature and time), and their Raman

521   spectra were taken. Then, the effect of changes in culture media, incubation temperatures and

522   times were also analyzed.[90] Another research carried out with *Bacillus* and *Brevibacillus*

523   species covered identification and differentiation of these bacteria with a UV-RR technique.

524   The researchers reaffirmed the accuracy of their results with analyses of 16S rDNA of the

525   bacteria. They stated that genotypic and phenotypic differences between microorganisms

526   could be detected by using characteristic Raman bands obtained from cellular components

527   such as aromatic amino acids and UV adsorption-capable nucleic acids. The spectra were

528   obtained at a wavelength of 244 nm, and subjected to multivariate statistical methods.[91] By

529   using FT-Raman system, Yang and Irudayaraj separated six different microorganisms (*S.*

530   *cerevisiae, Fusarium verticilliodes, Bacillus cereus, Aspergillus niger, Escherichia coli, L.*

531   *casei*) from each other as well as different strains belonging to the same species. They

532   reported differences due to cell structures within a 'fingerprint' range of 600-1800 cm^{-1} for

533   the microorganisms. PCA and CVA were used to characterize these microorganisms.[87]   In

534   another study by Maquelin et al., FT-IR and FT-Raman spectra were conducted on dehydrated

535   *Enterococcus faecalis*. C-H stretching bands belonging to (CH$_3$, CH$_2$, and CH) functional

536   groups were observed in the 2700–3000 cm^{-1} region, and the deformation band of the C-H

537   bond at 1450 cm^{-1} was also present. Protein amide I and amide II bonds and vibrations of

538   bases in RNA/DNA were also detected.[92] Colonies of *Microccoccus luteus* (*M. luteus*)*,*

539   *Bacillus subtilis* (*B. subtilis*)*, Pseudomonas fluorescens* (*P. fluorescens*)*, Rhodotorula*

540   *mucilaginosa* (*R. mucilaginosa*)*, and Bacillus sphaericus* bacteria were analysed with FT-

541   Raman. It was found that the spectra of *M. luteus, B. subtilis* and *P. fluorescens* had

542   completely different spectra from each other at a wavelength of 785 nm incident light. As a

543   result of stimulation with light at 633 nm, distinct templates were obtained from cells

544   belonging to the pigmented bacteria *M. luteus* and *R. mucilaginosa*.[86] The previously

545   mentioned group also seperated twenty different *Micrococcus*, *Bacillus*, *E. coli* and

546   *Staphylococcus* strains using micro-Raman spectroscopy coupled with SVM as chemometric

547   analysis.[90] Raman spectroscopy coupled with different chemometric methods was also used

548   for the identification of *Legionella*, *Klebsiella*, *Micrococcus*, *Bacillus*, *E. coli*, *Pseudomonas*,

549   *Staphylococcus*, *Listeria*, *Yersinia* and *Salmonella* species.[93-97]

550   Micro-Raman spectroscopy was also used to distinguish different types of *Lactarius*

551   mold by using chemometric methods. Lipid and amylopectin were monitored with Raman

552   spectroscopy since these are characteristic compounds for amyloidal reactions of *Lactarius*

553   spores. *Lactarius* mold is of great importance in ecological and economic sense and popular

554   in many regions of the world owing to its being edible.[98] Micro-Raman spectroscopy has also

555   been used to investigate the spatial distribution and composition of lipid vesicles inside intact

556   hyphae of *Mortierella* species. Differences in the degree of unsaturation and the effect of

557   growth conditions on lipid composition were determined for *Mortierella alpina* and

558   *Mortierella elongata* species.[99]

559

560   **Viruses**

561   There have been many studies reporting the use of Raman spectroscopy for structural

562   characterization of viruses. For instance, a number of studies have been conducted using

563   structural information obtained out of Raman spectroscopy to develop antiviral drugs.[100-103] In

564   one of these studies, the formation mechanism of the icosahedral capsid of P22 phage, which

565   is effective against *Salmonella typhimurium*, was tracked using a Raman microdialysis flow

566   cell. After preparation of the procapsid, empty shell, and scaffolding protein of the phage, all

567   the components were placed in the Raman microdialysis flow cell system and their Raman

568   signals were collected. The results were verified with Sodium Dodecyl Sulfate-

569   Polyacrylamide Gel Electrophoresis (SDS-PAGE) and the CD spectroscopy. In accordance

570   with their conclusions, researchers have managed to develop models for the transformation of

571   procapsid into capsid, and procapsid assembly.[102] UV-Raman has been used to investigate the

572   protein structure of another phage. Raman spectra of the phage were obtained by excitation at

573   four different wavelengths (257, 244, 238 and 229 nm). As a result of excitation at 257 nm,

574   signals of the bases that build the genome were obtained, and characteristic Raman bands

575   corresponding to the amino acids of the coat protein were attained as a result of excitation at

576   229 nm.[103, 104] Another research group has benefited from Raman optical activity (ROA) for

577   the structural characterization of nucleic acids, viruses and proteins in a manner disctinct from

578   other studies. The researchers found that working even with the full virus was possible, and

579   information on both the coat proteins, and the nucleic acids enclosed in the capsid could be

580   obtained.[100, 101]

581   There are very few studies on the analysis of foodborne viruses by using Raman

582   spectroscopy. Actually, there is a single study using Raman spectroscopy on Hepatitis A,

583   which is the most common foodborne virus.[105] Hepatitis A 3C proteinase is known to be a

584 cysteine protease which is very important for the life cycle of this virus and responsible for

585 the formation of mature viral proteins from the polyprotein precursor.[106] In the

586 aforementioned research, Raman spectra were used to investigate acyl groups in the active

587 site of the enzyme.[105] There have been several studies utilizing Raman spectroscopy for the

588 investigation of Hepatitis viruses, but none of them have been reported as a foodborne

589 virus.[107-109]

590

591 ## Raman spectroscopy for toxin and chemical detection

592 Contaminants are substances that have not been intentionally added to food. These substances

593 may be present in foods as a result of contamination in any stage of the production,

594 packaging, transport or storage. They can also result from the environmental contamination.

595 Since contaminants in general have a negative impact on the quality of food and are a threat to

596 human health[110], a number of analytical methods have been developed for the identification

597 and quantification of these compounds. Raman spectroscopy is one of these methods which

598 has gained increasing attention in recent years. Specific Raman bands related to toxin and

599 chemical detection were given in Table 6S.

600

601 **Toxins**

602 Brandt et al. aimed to study the structural properties of the toxins ricin, ricin agglutinin and

603 ricin binding subunit B. Ricin and ricin agglutinin were extracted from *Ricinus communis*

604 seeds and purified using affinity chromatography and gel-filtration. Vibrational bands of this

605 plant toxin were then obtained by using Raman spectroscopy. Amide I at 1640 cm^{-1}, amide III

606 at 1210–1300 cm^{-1}, a tyrosine doublet at 830 and 855 cm^{-1}, bands for disulphide bridges at

607 510, 525 and 540 cm^{-1}, and some several bands corresponding to tryptophan amino acid

608 residues at 1361 cm^{-1} were used as conformation sensitive bands for the molecules of

609 interest.[111]

610   In another study, several vegetables and fruits were analysed with micro-Raman and

611 near-infrared FT-Raman spectrometry to detect trace amounts of residual pesticides on the

612 surface.[112] Bonora et. al., investigated the Raman spectra of atrazine, prometryn and simetryn

613 herbicides in solid form and in polar and apolar solvents. A comparison was made between

614 theoretical spectra and experimenta spectra obtained from Raman and Surface-enhanced

615 Raman spectroscopy (SERS) measurements.[113] In a similar study, Fleming et. al. investigated

616 the molecular structure of phosphorus-containing herbicides. IR, Raman and SERS spectra

617 were collected and compared with Density Functional Theory (DFT) calculations.[114]

618   Deoxynivalenol (DON) is one of the major secondary metabolites of the *Fusarium*

619 genus and found predominantly in grains such as wheat, barley and corn.[115] The presence of

620 DON degrades the quality of grain and has toxic effects on human health.[116] Traditional

621 methods to measure DON concentrations in grain involve time-consuming steps such as

622 extraction, washing and binding.[117] Due to the high moisture content in grain, broad intense

623 water bands are yielded in both the IR and NIR regions. Thus, highly informative bands

624 attributable to carbohydrate and protein species are inhibited. For this reason, various kinds of

625 studies have been conducted with IR spectroscopy. The only study in the literature for

626 identification of DON toxin by using a Raman technique with infrared spectroscopy was

627 published by Liu et al.. In this study, feasibility of FT-Raman spectroscopy for the

628 characterization and classification of ground wheat and barley contaminated with varying

629 amounts of DON was investigated. PCA was performed in the spectral region 1800–800 cm^{-1}

630 for multiplicative scatter correction of the Raman spectra. Principal component scores were

631 then examined to discriminate between low and high DON in wheat.[118]

632   Raman spectroscopy coupled with LDA was used for qualitative and quantitative

633   analysis of aflatoxin produced by *Aspergillus* in maize. Differences in the Raman bands were

634   observed depending on the aflatoxin concentration in the samples.[119] In another study carried

635   out by Lee et al., three different vibrational spectrophotometric methods, namely Raman, FT-

636   NIR, and FT-IR were used for the detection of alfatoxin in different concentrations. By

637   applying different chemometric methods to the spectra obtained from these three methods, a

638   classification was made according to their alfatoxin quantities. The researchers stated that

639   based on the results of the chemometric method they applied, Raman and FT-IR analyses had

640   given relatively more satisfactory results compared to FT-NIR.[120]

641   In a study by Gupta et al., in situ synthesis of a nanopatterned conjugated molecularly

642   imprinted polymer for bioagent T-2 on a bare gold chip and its integration with surface

643   plasmon resonance and Raman spectroscopy were explored. The p-aminophenylboronicacid

644   (p-APBA) and p-APBA with T-2 were characterized with Raman spectroscopy. Upon

645   polymerization of 3-APBA with T-2, the presence of new bands was detected, and they were

646   assigned to symmetric B-O and asymmetric C-O stretching modes for p-APBA and T-2 in the

647   sample.[121]

648

649   **Chemicals**

650   Coumarin is a naturally occurring benzopyrone found in most plants including tonka beans,

651   sweet clover, woodruff and grass. It was used as a flavouring food additive until its direct use

652   was banned due to the concerns about hepatotoxic effects on animal models.[122] Sortur et al.

653   reported that IR and Raman spectra of 6-methyl-4-bromomethylcoumarin were obtained by

654   following the reaction of *p*-cresol with 4-bromoethyl acetoacetate on an ice bath.[123]

655   Bisphenol A (BPA) is an estrogenic compound widely used in polycarbonate plastics,

656   food cans and food storage containers.[124] Dybal and co-workers prepared BPA samples by

657   varying thermal and solvent treatments. Characteristic amorphous bands at 735 and 1235 cm^{-1}

658   were used to determine the degrees of crystallinity of the BPA polycarbonate samples.[125]

659   Ground waters may be contaminated with perchlorate ions originating from the use of

660   fertilizers and manufacturing activities. Levitskaia, Sinkov and Bryan used perchlorate loaded

661   ion exchange resin as their model system. Determination of perchlorate with Raman

662   spectroscopy was found to be a practical real time detection method. Perchlorate, a tetrahedral

663   anion possessing easily polarizable Cl-O bonds, exhibits a vibrational frequency of the

664   symmetric stretch near 934 cm^{-1} in aqueous solution. The ClO_4^- bands were normalized to the

665   intensity of the prominent A850 resin band at 1452 cm^{-1} that served as an internal standard.[126]

666   Yu et. al used RR spectroscopy for quantitative analysis of divalent metal ions.[127] Chelation

667   property of zincon molecule with Cu^{2+} and Ni^{2+} enabled researchers to obtain complexes

668   which could be followed by RR spectroscopy.

669   Polycyclic aromatic hydrocarbons (PAH) constitute a potential health danger because of

670   their ability to induce carcinogenesis. PAH (such as napthalene, anthracene, phenanthrene,

671   and pyrene) could be detected in trace levels by making use of UV-RR spectrometry. A strong

672   band for naphthalene was located at 766 cm^{-1}. Other strong bands were observed at 399, 756

673   and 1407 cm^{-1} for anthracene, at 386, 745 and 1386 cm^{-1} for phenanthrene and at 582, 1393,

674   and 1622 cm^{-1} for pyrene.[128] Alajtal, Edwards and Scowen used FT-Raman spectroscopy to

675   investigate the effect of spectral resolution on the Raman spectra of several polyaromatic

676   hydrocarbons. In this study, Raman measurements of beta-carotene naphthalene, β-carotene

677   anthracene, β-carotene pyrene, and naphthalene, anthracene, and pyrene molecules were taken

678   with different spectral resolutions. The effect of spectral resolution on the obtained Raman

679   spectra was evaluated in this study.[129]

680   In the study of Sundaraganesan, Puviarasan and Mohan, the vibrational spectra of

681   acrylamide found in starchy food products as a result of cooking practices was discussed in

682   detail with respect to various environments. A complete vibrational assignment using

683   polarization data along with the results of normal coordinate analysis were presented in this

684   study by taking into account the internal modes of the CH_2 and NH_2 groups.[130]

685

686   **Raman spectroscopy in food additive analysis**

687   Raman spectroscopy has also been used to detect food additives, and different approaches

688   have been taken into account for this purpose. Specific Raman bands for food additive

689   analysis section were given in Table 7S.

690   Astaxanthin (E-161j) and cantaxanthin (E-161g), the two major carotenoids responsible

691   for the red-orange colour of salmon, were investigated by using Raman spectroscopy. Strong

692   Raman signals were observed as a result of the C=C stretch vibrations of the carotenoid

693   molecules.[131] Carbon black (E-153), another colouring agent which is produced by the

694   combustion of hydrocarbons, was analysed with Raman spectroscopy.[132] Snehalatha et. al.,

695   investigated the molecular structure of amaranth (E-123), a commonly used colouring agent

696   of the food industry. Most characteristic bands were assigned to the vibrations of naphthalene

697   ring and azo chromophoric group (C-N=N-C). A medium intensity band in the Raman

698   spectrum was identified as the symmetric stretching vibration of the SO_3 group. The strongest

699   Raman band was obtained out of the naphthalene ring vibrations.[133] Peica et. al. studied the

700   molecular structure of tartrazine (E-102), an artificial dye which is also known for its potential

701   to cause allergic reactions. Its strongest bands resulted from the azo and carboxyl groups and

702   C-H deformation of the phenyl groups.[134] Curcumin is a natural coloring agent and

703   stabilizator in the food industry as it is the major contributor to human health, yet it has a

704   limited application area because of its low solubility and stability. To enhance solubility and

705   stability of curcumin, encapsulation was applied with cyclodextrin, and then characterization

706   of this complex was accomplished with Raman spectroscopy. The researchers showed that

707   Raman spectra of curcumin-cyclodextrin complex were different from Raman spectrum of

708   curcumin.[135]

709   Zborowski et. al., used IR and Raman spectroscopy for characterizing the molecular

710   structure of maltol which is widely used as a natural food additive. Maltol was characterized

711   with its strong band related to the O-H stretching.[136] Peica et. al. used Raman spectroscopy to

712   investigate the molecular structure of monosodium glutamate which is a commonly used

713   flavour enhancer in various food products. Strong Raman bands were explained by CH_2

714   stretching, COO^- stretching, CH_2 deformation, completely ionized form, and COO^-

715   twisting.[137] In another study by Peica et. al., aspartame (E-951) as an artificial sweetener was

716   analysed by using Raman spectroscopy. Strong Raman bands were assigned to symmetrical

717   C-H phenyl ring stretching, in-plane C-H phenyl ring bending, symmetrical stretching,

718   phenylalanine ring stretching, CH_3 rocking, and skeletal deformation.[138]

719   Potential of IR, Raman and SERS to determine the excess azodicarbonamide additive in

720   flour samples was evaluated. Its reaction products, namely biurea and semicarbazide that were

721   formed during baking process were monitored by following their characteristic Raman

722   spectra. Although multiple characteristic Raman bands were observed for each product, their

723   presence is mostly assigned to the deformation bands of NH_2, stretching and bending

724   vibrations of N-C and C=O bounds. Results taken from experimental and calculated Raman

725   spectra were verified with DFT.

726   Another food additive, chitosan, which is obtained by deacelitation of chitin, is of

727   great importance since the degree of its deacetilation is vital in order to determine its chemical

728   and physiccal properties such as solubility, biodergradibility and biocompatibility.[139] In this

729   respect, Zajac et al. demonstated that the deacetilation degree of chitosan could be calculated

730   by following certain bands obtained from Raman and IR spectra related to it.[140] The other

731   chitosan derivative obtained by sulfating are known to have anticoagulant, antiviral,

732   antimicrobial, and antioxidant characteristics. It could be possible to determine the degree of

733   substitution and to characterize sulfated chitosan compounds using Raman spectroscopy.

734   Changes due to binding of sulfate groups to chitosan were detected in the obtained Raman

735   spectra (1070, 1014, 823-834, 580-610, 2964 cm^{-1}) and these compounds were characterized

736   according to the amount of the sulfate group attached to the structure.[141]

737   Another food additive is mannitol, which is used in the production of low-calorie food,

738   as well as in the pharmaceutical industry and in other lyophilized products. In a study,

739   changes occurring in the bands of ice, water and mannitol during the lyophilization of

740   mannitol, were examined. Raman bands of ice and mannitol were monitored at the spectral

741   regions 150-250 cm^{-1} and 1000-1170 cm^{-1}, respectively. Different polymorphic forms of

742   mannitol were displayed during the lyophilization process.[142]

743

744   Raman spectroscopy in raw material analysis

745   Rapid and *in situ* analysis of raw materials is one of the most important quality control

746   applications in food industry. Assesing the quality of raw materials before the food production

747   phase helps manufacturers save time and reduce the cost. Identification of raw materials is

748   also essential due to its major effect on the quality of final product. Taking these requirements

749   into account, it can be stated that Raman spectroscopy provides a wide range of applicaion

750   area in which the raw material analysis constitutes a significant part. In this context, Raman

751   spectroscopy has been widely used for raw material analysis, particularly for the

752   discrimination of food samples, monitoring chemical and biochemical processes,

753   compositional characterization of food samles and authentication of foods. Nevertheless,

754   analyzing the Raman spectra of food samples mostly requires chemometric tools because of

755   the complex structure of food matrix. Unsupervised chemometric methods like Principal

756   Component Analysis (PCA) and supervised chemometric methods like Partial Least Square

757   (PLS), Partial Least Square-Discriminant Analysis (PLS-DA), Principal Component

758   Regression (PCR) as well as Artificial Neural Networks (ANN) were generally employed for

759   the detailed analysis of collected Raman data.[143-146] Specific Raman bands reported in the

760   context of the reviewed articles is given in Table 8S for raw material analysis.

761

762   **Honey**

763   In a study by Goodacre, Radovic and Anklam, Raman spectroscopy was used with PCA and

764   ANN to discriminate between honey samples provided from various European countries with

765   different floral and geographical origins.[144] First, scores representing the Raman spectra of

766   honey samples were obtained and then ANN, which was created from these scores, was used

767   for discrimination. According to the results, 13 of 14 honey samples were classified

768   accurately, but the country of origin was not predicted successfully as the number of honey

769   samples was insufficient. Another research on honey has also recently been carried out by

770   Özbalci et al. In this study, sugar contents of honey samples were quantified by applying

771   chemometric methods to Raman spectra of honey samples.[147] Similar to the first study

772   mentioned in this review, Carvucci et al. discrimated the honey samples collected from

773   different regions by using Raman spectroscopy. They processed the Raman spectra that they

774   obtained according to the pollen composition of genuine honey by using PCA, and identified

775   the botanical and geographical origins of it.[148]

776

777   **Coffee**

778   There are three studies in the literature conducted for discriminating between Arabica and

779   Robusta green coffee by using Raman spectroscopy.[143, 149, 150] The reason for the researchers

780   to discriminate these two kinds coffee is that their quality, and thus price is not the same.

781   Analyzing their lipid content was the focus of these studies, and it was found that especially

782   their kahweol content considerably differs from each other. The first Raman study on this

783   topic of interest was carried out by using FT-Raman spectroscopy. The researchers obtained

784   Raman spectra of lipid samples (kahweol and cafesto) extracted from coffee samples. Two

785   characteristic peaks (1567 ve 1478 cm^{-1}) of kahweole were found in the extract taken from

786   Arabica coffee, which is specific to this type of coffee. They also discriminated between these

787   two coffee types with a success rate of 93% by using chemometric method PCA.[150] Similarly,

788   in a subsequent study, these two kinds of coffee were discriminated by using FT-Raman.

789   However, it differs from the former study in that Raman spectra of the samples were taken

790   without applying any chemical and physical procedure on the coffee beans. The discrimation

791   of the coffees was performed by calculating the "spectral kahweol index" with the spectra

792   obtained from the samples with different geographical origins.[149] In another study,

793   chlorogenic acid rate was also examined as well as the lipids present in Arabica and Robusta

794   green coffee. Raman spectra of the samples were obtained with visible micro-Raman

795   spectroscopy; and by using two different PCA models, the discrimiation of the coffees were

796   accomplished with a success rate of 93%.[143]

797

798   **Lipid**

799   A study on discrimination among different edible oils and fats was performed by Yang et al.

800   In this study, spectra obtained from FT-Raman spectroscopy were compressed with PLS and

801   PCA; then the processed data were used for Linear Discriminant Analysis (LDA) and

802   Canonical Variate Analysis (CVA). As a result of the analyses performed using the spectral

803   range between 400 and 3700 cm^{-1} (Table 1S), PLS-CVA was found to be the best method for

804   discriminating edible oil and fats by FT-Raman, with calibration and validation data of 93.3%

805   and 94.4%, respectively.[68] Korifi et al. tried to evaluate the capability of confocal Raman

806   spectroscopy combined with chemometric treatments to authenticate virgin olive oils with the

807   protected designation of origin (PDO) label. Hence, PLS-DA was applied to the spectra of

808   eight French PDOs, and 92.3% of these oils were accurately classified.[151] Raman

809   spectroscopy has also been used to determine the quality of the olive fruit, which is one of the

810   most important quality parameters in olive oil processing. In another study on olive oil, it was

811   put forward that low-resolution portable Raman system could be utilized for determining

812   oxidation states of oils. Having benefited from a chemometric method (PLS), the researchers

813   stated that due to oxidation, changes occurred in the bands at about 1267, 1302, 1442, 1655 ve

814   1747 cm^{-1}.[71] They also tried to determine the quality of olive oil by using the Raman spectra

815   of ground or sound olive paste, and then attempted to discriminate the origin of the olives as

816   ground or sound. In the first stage of the study, PCA was used to find natural clusters in the

817   Raman spectra, and then supervised classification methods, namely Soft Independent

818   Modelling of Class Analogy (SIMCA), PLS-DA and *K*-Nearest Neighbors' (KNN) were

819   applied. The best results for classification were found in the KNN method, with prediction

820   abilities of 100% for sound and 97% for ground olives in an independent validation set. In this

821   study, it was demonstrated that portable Raman spectroscopy can be utilized to determine the

822   quality of olives used in the production of olive oils in the field.[152] Different from the other

823   studies on olive oil, Gouvinhas et al., produced extra virgin olive oil by means of taking

824   samples from three types of olive in different stages of their ripening periods. They were

825   classified according to their types and ripening periods through processing the Raman spectra

826   with qualitative methods. It was found that 1749, 1651, 1439, 1303 ve 1267 cm^{-1} bands

827   obtained from Raman measurements directly demonstrates the fatty acid contents of the

828   samples, and changes were observed in the intensities due to ripening.[153]

829

830   In another study, different types of pure animal fat (poultry, pig, bovine, and lamb and

831   fish oils) and mixture samples of them were classified according to their origin by using PCA

832   and PLS-DA analyses.[66] The same analysis was performed with different types of edible fats.

833   Fish, poultry, pig and bovine fats were well distinguished by applying PCA. Using PLS-DA

834   analysis, poultry, pig and bovine fat samples were discriminated with high sensitivity and

835   specificity values and with few classification errors. In addition, types of edible fats like fish

836   oils and acidic oils from chemical or physical refining could also be discriminated with PLS-

837   DA.[66] Velioğlu et al., used Raman spectroscopy to assess the freshness of fish samples

838   according to the number of freezing/thawing cycles they were exposed to. PCA was employed

839   to cluster the samples according to their freshness. Changes in the intensities of the

840   characteristic Raman bands were mostly attributed to the alterations in the lipid structure.[154]

841   Potential of Raman spectroscopy to predict the purity of caviars was evaluated. Linear

842   methods such as PCA and LDA as well as non-linear methods such as ANN were used to

843   classify different caviar samples according to their purity and type. More accurate predictions

844   were obtained by using the ANN with 91.4% of prediction capability. Fatty acids and fat

845   contents of the caviar samples was quantified through Raman spectroscopy coupled with PLS

846   regression.[155]

847   In addition to the abovementioned studies on lipids, there is another study in which

848   Raman spectra of 35 lipids belonging to different families (saturated and unstaturated fatty

849   acids, triacylglycerols, cholesterol, cholesteryl esters and phospholipids) were obtained. It was

850   found that Raman spectra of each of these lipids display changes depending on their

851   saturation state, their being in liquid and solid state, and on isomer forms. The characteristic

852   features of Raman spectra is attributable to the existance of hydrocarbon chains, and they

853   were observed at 1500-1400, 1300-1250, 1200-1050, 3000-2800 cm^{-1}, respectively, which

854   was caused by C–C and C–H stretching modes and the scissoring and twisting vibrations of

855   CH$_2$ and CH$_3$ groups. Besides, lipids belonging to each group was found to have characteristic

856   bands specific to them.[156]

857

858   **Fermentation products**

859   Raman spectroscopy can also be used to detect materials such as ethanol, lactic acid, and

860   acetic acid that are produced as a result of processes like fermentation. Sivakesava et al.,

861   followed ethanol fermentation by *Saccharomyces cerevisiae* (*S. cerevisiae*) using Fourier

862   Transform-Middle Infrared (FT-MIR) and FT-Raman spectroscopy. In this study, quantities

863   of glucose, ethanol and the optical cell density of *S. cerevisiae* during fermentation were

864   investigated using chemometric methods.[157] In another study, FT-MIR, Fourier Transform-

865   Near Infrared (FT-NIR) and FT-Raman spectroscopy were used during lactic acid

866   fermentation to determine quantities of the same parameters as the previous study of

867   *Lactobacillus casei* (*L. casei*).[158] Similarly, quantitative measurements of glucose during

868   ethanol fermentation in the beverage industry were carried out by Delfino et al.[37] Our research

869   group has also monitored a two-step acetic acid fermentation in a study using Raman

870   spectroscopy. The first step was consumption of sugars in a grape juice mixture and then

871   formation of alcohol by *S. cerevisia.* The second step was carried out with *Acetobacter aceti*

872   that converted the alcohol to acetic acid.[159] Wang et al. used Raman Spectroscopy to monitor

873   the consumption and formation of glucose, glycerol and ethanol during wine fermentation.

874   HPLC was used for the validation analysis.[160] Micro-Raman spectroscopy was used to follow

875   the fermentation process during yoghurt production. Chemical transformation of lactose and

876   inorganic phosphorus into lactic acid and organic phosphorus and the formation of the

877   exopolysaccharides were monitored based on the collected Raman spectra as a function of the

878   incubation time.[161]

879

880 **Other foods**

881 A dispersive Raman spectroscopic method was developed to determine protein and oil

882 contents of soybeans.[162] Optimal prediction models were generated by PLS algorithms based

883 on collected Raman spectra (200-1800 cm^{-1}) of the samples. Protein and oil content of the

884 soybeans were succesfuly predicted with high R^2 values (0.916 and 0.872 for protein and oil

885 contents, respectively). Characterization of foods is another topic studied by using Raman

886 spectroscopy. For this purpose, FT-Raman spectroscopy was used for the characterization of

887 Marama beans from Southern Africa. Both quantitative and qualitative data on the

888 composition of Marama bean oil, including carbohydrates, proteins, amino acids and aromatic

889 compounds, were obtained.[145] Ripe and unripe tomato fruit samples were analyzed with

890 portable and confocal Raman microscope to obtain spectral data on their main organic

891 components. Two different laser excitation wavelengths were used for confocal microscope

892 measurements to maximize the obtained spectral information.[163] By using spectral data, cutin

893 and cutinal waxes on unripe tomatoes and carotenes, and polyphenoles and polysaccharides

894 on ripe tomatoes were identified as major compounds. In another study, the researchers traced

895 the lycopene formation and distribution in the structures of the harvested tomatoes during

896 different stages (green, breaker, turning, pink, light red, red) of their ripening period by using

897 Raman chemical imaging. Tomatoes in different ripening periods were cut parallel to the

898 plane, and Raman spectra were taken from their seeds, locular tissues and outer pericarps. As

899 a result of the trials, two basic peaks (1151 and 1513 cm^{-1}) belonging to lycopene were

900 detected both in locular tissues and on outer pericarps of fully ripened (red) tomatoes.[164]

901 Gonzalves et. al., used transmission resonance Raman spectroscopy to investigate the spatial

902 distribution of carotenoids in carrot roots, and they found that the changes in the intensities of

903 Raman bands obtained from different parts of carrots were attributed to molecular

904   configuration of β-carotene. As a consequence, β-carotene showed a heterogenous

905   distribution, and seen particularly in the secondary phloem tissue, and periderm.[165]

906   Raman spectroscopy can also be used to monitor important components such as ethanol,

907   lactic acid, and acetic acid produced during fermentation[166,167] and/or spoilage of foods[168] and

908   chemical and biochemical transformations.[169, 170]

909

Raman spectroscopy to detect food adulteration

910

911   Food is adulterated by unscrupulous producers in order to benefit economically from

912   falsifying food information. The development of new techniques to verify food safety and

913   authenticity has been an important issue thanks to the increasing consumer awareness.[1] For

914   this reason, rapid and eco-friendly techniques have replaced time-consuming and tiresome

915   chemical and traditional reference methods. As a vibrational technique, Raman spectroscopy

916   is one of the analytical tools and is attracting growing attention due to its ability to provide

917   fingerprint characteristics of food products and its offering a rapid, non-destructive and cheap

918   analysis. In addition, quantitative and qualitative information can be obtained from a

919   combination of Raman spectroscopy with multivariate data analyses.[171] Specific Raman bands

920   of related articles to this section were given in Table 9S for food adulteration.

921   Zou et al. used a portable Raman spectroscopy to distinguish between genuine olive oil

922   and the oil adulterated with low quality oils. A method was developed based on the

923   normalization of *cis*-(=C-H) and *cis*-(C=C) bands intensities at 1265 cm^{-1} and 1657 cm^{-1}, by

924   the CH_2 band intensity at 1441 cm^{-1}. Adulterated olive oil containing as little as 5% (v/v) or

925   more of other edible oils have been successfully detected in the relevant study.[172] Zhang et al.

926   investigated extra virgin olive oils adulterated with soybean, corn or sunflower seed oil by

927   characterizing their Raman spectra in the 1000–1800 cm^{−1} range. The Raman spectra were

928   normalized according to the CH_2 band of the oil samples. An external standard method (ESM)

929 was applied to achieve quantitative analysis and compared with the results of SVM methods.

930 Potential of ESM based on Raman spectroscopy to detect olive oil adulteration was shown in

931 this study.[173] In another study of Zhang et al., the level of adulteration in a set of olive oil

932 samples containing 5% or more of different types of oils such as soybean, rapeseed, sunflower

933 and corn oil was successfully determined. Using PCA made it possible to obtain a clear

934 separation of oil samples according to their different mono-unsaturated fatty acid,

935 polyunsaturated fatty acid, and saturated fatty acid contents.[174] Lopez-Diez et al. also

936 investigated the authentication of various extra virgin olive oils, and their adulteration with

937 hazelnut oil by using Raman spectroscopy. The obtained Raman spectra were normalized

938 according to the frequency of the band representing the scissoring-bending mode of $-CH_2$

939 groups. The spectra were examined by using PCA, PLS and Genetic Programming. Extra

940 virgin olive oils from different parts of the Italian peninsula and their mixtures with hazelnut

941 oils were characterized using PCA. The PLS method was also used as a predictive linear

942 model.[175] El-Abassy et al. studied visible Raman spectroscopy to classify different vegetable

943 oils and quantify the adulteration of virgin olive oil with sunflower oil. PCA was used for the

944 classification study, while PLS regression analysis was used to monitor the adulteration.

945 Quantitative detection limit was decreased to 500 ppm (0.05%), which is significant in the

946 case of allergic reactions.[176] Adulteration of extra virgin olive oil with olive pomace oil was

947 determined by means of NIR, FT-IR and FT-Raman spectroscopy. PLS was used to

948 quantitatively analyse the olive oil samples adulterated with different rates of olive pomace

949 oil.[177] Baeten and Aparicio conducted European project FAIR-CT96-5053, which evaluated

950 the performance of FT-Raman, NIR and FT-MIR spectroscopy to authenticate one-hundred

951 thirty-eight different edible oil and fat samples.[178] PCA and stepwise linear discriminant

952 analysis (SLDA) methods were performed to classify oils and fats by conducting cluster and

953 discriminant analyses. Three clusters of samples that were rich in saturated fatty acids,

954   monounsaturated fatty acids or polyunsaturated fatty acids were obtained with PCA according

955   to the degree of unsaturation of the oils. In another method, SLDA was performed to classify

956   edible oils and fats according to their sources, and to quantify virgin olive oil adulteration. In

957   one of the studies reported by our research group, Raman spectroscopy was used to detect the

958   adulteration in butter samples spiked with margarine. Prediction success of the models

959   created by using different chemometric methods namely PCA, PCR, PLS and ANN were

960   compared.[179]

961   Adulteration of milk powder with melamine was determined quantitatively by using

962   portable Raman spectroscopy coupled with PLS regression. Melamine adulteration was

963   monitored using the characteristic bands of melamine located at one strong band at 673 cm^{-1}

964   and a weak band at 982 cm^{-1}. The intensity of the band at 673 cm^{-1} was used for quantification

965   of melamine concentration in milk powder.[180] In a similar study, adulteration of milk powder

966   with melamine was examined using the melamine band located at 676 cm^{-1}.[181] Adulteration

967   was successfully determined in the milk powder samples spiked with calcium carbonate.

968   Prominent peak of calcium carbonate located at 1085 cm^{-1} was followed in FT-Raman spectra

969   of milk powder samples. PCA and PLS was used with Raman spectroscopic data to quantify

970   the adulteration rate.[182] Multiple adulterants, namely ammonium sulphate, dicyandiamide,

971   melamine, and urea present in the milk powder samples were simultaneously detected by

972   using Raman chemical imaging coupled with mixture analysis algorithms. Differences in the

973   Raman spectra of four chemical adulterants allowed researchers to detect and differentiate

974   these compounds. The strongest Raman bands characterizing the relevant chemical

975   compounds were as follows; 973 cm^{-1} for ammonium sulphate, 212 cm^{-1} for dicyandiamide,

976   673 cm^{-1} for melamine and 1009 cm^{-1} for urea.[183]

977   Adulteration of maple syrup with corn syrup has been investigated using FT-IR, FT-

978   Raman and NIR spectroscopy. Quantitative analyses of adulterated samples were performed

979　with PLS. PCA-LDA, PLS-CVA, PLS-LDA and PCA-CVA methods were also applied for

980　discriminant analysis, but the best results were obtained with PCA-CVA. Characteristic bands

981　mostly attributed to the presence of carbohydrates were used for creating above-mentioned

982　predictive models.[184]

983　　　　Adulterated honey samples with various floral origins containing beet and cane inverts

984　were successfully determined using FT-Raman spectroscopy coupled with PLS and PCA

985　combined with CVA and LDA.[146]

986　　　　Detection of paraffin in the adulterated rice samples was investigated. Confocal

987　microscope Raman measurements were performed on the surface of rice samples to obtain

988　information about chemical composition. PCA, SIMCA, PLS-DA, KNN and SVM methods

989　were used to differentiate rice samples from different locations and to detect paraffin in the

990　adulterated rice samples. Although the Raman spectra of rice samples comprised of starch,

991　protein and lipid, researchers were also able to detect the presence of paraffin by following

992　the strong Raman bands at 1062, 1132, 1295, 1417, 1440 and 1462 cm^{-1}.[185]

993　　　　Methanol and ethanol content of distilled alcoholic beverages was successfully

994　determined with Raman spectroscopy. Quantification of methanol in mixtures was done using

995　the intensities of methanol and ethanol bands located at 1019 and 879 cm^{-1}, respectively.

996　Collected Raman data was normalized by using acetonitrile as an internal standard in the

997　developed method.[186] Nguyen and Wu developed a Raman spectroscopic method to quantify

998　low concentrations of methanol in alcohol. PLS regression was applied to the collected

999　Raman spectra where spectral region between 950 and 1200 cm^{-1} was specifically used to

1000　obtain the calibration curves.[187]

1001　　　　Identification of meat species is of great importance in order to determine the potential

1002　adulteration of meat products with cheaper alternatives. Beattie et. al., used Raman

1003　spectroscopy and multivariate data analysis to classify adipose tissue samples from different

1004   origins. PLS-DA and PC-LDA were employed to classify the samples of chicken, beef, lamp

1005   and pork species.[188] Sowoidnich et. al. used shifted excitation Raman difference spectroscopy

1006   for the non-invasive differentiation of meat species, namely beef, pork, chicken and turkey. A

1007   clear separation was obtained by employing PCA to the collected Raman data.[189] Boyaci et.

1008   al., used Raman spectroscopy in combination with chemometrics to determine the beef

1009   adulteration with horsemeat. Employing PCA on collected Raman data enabled researchers to

1010   differentiate beef samples spiked with different rates of horsemeat.[190] In a similar study

1011   reported by the same research group, extracted fat samples were used to differentiate meat

1012   species namely, cattle, sheep, pig, fish, poultry, goat and buffalo. Salami products with

1013   different formulations prepared by using these meat species were also investigated with

1014   Raman spectroscopy.[191] Zajac et. al. used IR and FT-Raman spectroscopy to analyze the

1015   amino acid composition of the samples in order to determine the content of horse meat in its

1016   mixture with beef.[192]

1017

1018   Conclusion

1019   The use of Raman spectroscopy in food analysis is still in its initial stage despite its great

1020   potential in almost every field of food science. Raman has many advantages compared to

1021   other food analysis methods, and the use of Raman is increasing day by day. Raman

1022   spectroscopy can replace traditional food analyses as it does not require labelling and pre-

1023   treatment steps. In addition, Raman spectroscopy is a sensitive, reliable, non-destructive and

1024   real-time method. Some important issues that need to be addressed for making Raman

1025   spectroscopy a more commonly used method are:

1026   *a. Investigating the applications for Raman spectroscopy in food analysis.* Due to some

1027   reasons (cost and scarcity of the instrument in food area etc.), the usage of the Raman

1028   system in food analysis didn't use to be a common practice. Over the last two decades,

however, these limitations have been partially eliminated, and the number of reported

studies in this field has increased. Nevertheless, it is still not sufficient and more studies

should be conducted. Results of the Raman system should be correlated with standard

methods, and new standard methods should be developed using Raman spectroscopy.

According to our detailed research on the literature, some aspects of food analysis still

need to be investigated by using Raman spectroscopy. To our knowledge, mineral and

toxin analysis in food studies are among these aspects waiting to be dealt with using

Raman spectroscopy.

b. Application-driven databases for common analysis. Although some studies have been

carried out in this field, there is still no available database related to Raman

spectroscopy in food analysis. Complex food matrices and variations in the systems

cause difficulties in preparation of databases. In this review, Raman bands obtained in

food analyses were summarized in tables (Table 1S-9S). We believe that these tables

will be beneficial for researchers in this field. However, more systematic experimental

work is needed for the preparation of this database. The Raman system's becoming

more widespread in food field will help develop a database.

c. Improving analysis efficiency. The complex nature of the food sample reduces

efficiency of the analysis. To overcome this difficulty, some easy preprocessing

practices could be conducted before Raman measurement. In addition, novel data

processing techniques (chemometric methods and artificial neural networks) will be of

more help to the user, and processing Raman spectra with these methods will increase

the efficiency of the analysis.

d. Better analyser instrument. Most of the Raman systems were developed for the

research purposes in laboratories. There is no individual Raman system for specific food

analysis. The success of Raman spectroscopy in food analysis will be increased through

developing individual Raman systems. Field assays are also very important in food analysis. Portable Raman systems have big potential in this field. Developments in light source and detector technologies will help produce small size portable Raman modules with better performance.

e. Low cost analyser system. High cost of Raman modules obstructs the common usage of the system in this field. Simpler systems, designed specifically for the sample and portable Raman system should be produced with lower instrumentation cost.

Raman spectroscopy in food analysis is receiving a lot of interest from researchers worldwide. We believe that Raman spectroscopy will be one of the most common methods to be used in food analysis in the near future.

SUPPLEMENTARY DATA AVAILABLE

Supplementary data including the tables displaying the Raman bands of food components (proteins, carbohydrates, lipids, and vitamins), microorganisms and viruses, toxins and chemicals, food additives, raw materials and food adulterant is available.

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1344   **FIGURE LEGEND**

1345

1346   Fig.1. Energy level diagram of Rayleigh and Raman scattering.

1347   Fig.2. Schematic presentation of fields in food analysis in which Raman spectroscopy used.

Figure 1.

Figure. 2.