



Effect of microwave treatment on metal-alginate beads



Laura Campañone^{a,b,*}, Estela Bruno^{a,c,d}, Miriam Martino^a

^a CIDCA (Centro de Investigación y Desarrollo en Criotecología de Alimentos), CCT La Plata, CONICET, Facultad de Ciencias Exactas, UNLP, Calle 47 y 116, La Plata 1900, Argentina

^b Departamento de Ingeniería Química, Facultad de Ingeniería, Universidad Nacional de La Plata (UNLP), Argentina

^c Facultad de Ciencias Veterinarias, Universidad Nacional de La Plata, La Plata 1900, Argentina

^d CIC (Comisión de Investigaciones Científicas de la Pcia. de Buenos Aires), La Plata 1900, Argentina

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ABSTRACT

Encapsulation is defined as a technique to protect solid, liquid or gaseous active compounds from interacting with the environment. Encapsulated minerals may be incorporated into food products submitted to microwave heating, thus it is interesting to study their interaction with microwaves due to the relevant dielectric properties of the ions during heating. In the present work, zinc sulphate heptahydrate, ferrous sulphate heptahydrate, calcium chloride and sodium alginate were used to test metal ion-alginate beads under microwave heating. The objective was to compare the behavior of free ions in solution with those trapped within the alginate matrix while being submitted to electromagnetic radiation. The beads were characterized before and after heating by texture profiles, differential scanning calorimetry and infrared spectroscopy (FTIR). During microwave heating, the presence of zinc and iron increased the inner temperature of the system; however calcium did not show the same behavior. These differences were attributed to the microstructure of the beads.

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1. Introduction

Encapsulation is a process in which a thin polymer coating is formed around solid particles, liquid droplets or gases that are fully contained within the capsule walls. In some cases a minimum amount of the active material can remain exposed at the surface (Sahidi and Han, 1993; Deladino et al., 2008). In the food industry, encapsulation not only allows adding value to a food product, but also becomes a source of new additives with unique properties.

Alginic acid is a linear polysaccharide made up of α -L-guluronic acid and β -D-mannuronic acid. It is extracted from brown seaweeds and its sodium salt is a water-soluble polymer. Sodium alginate has been employed to make gel beads for the delivery of biomolecules such as drugs, peptides and proteins. Divalent cations bind preferentially to the guluronic blocks in the alginate in a highly cooperative way, thereby forming a gel (Wong et al., 2002).

Iron and zinc are two of the most important minerals for human nutrition. Iron plays an important role in human life, being essential in the oxygen transport and cellular respiration process. The human body takes this element from the diet by several ways

according to its necessities. Besides, zinc is a trace element, indispensable for human health. It is essential for the body defense, plays an important role in the growing and division of the cells (Sarubin Fragaakis and Thomson, 2007).

Bearing in mind that these elements are needed for organic functions, their encapsulation would allow increasing their daily intake without modifying the original flavor of the preparations (Gouin, 2004; Tannenbaum and Young, 2005; Desai and Jin Park, 2005; Sun-Waterhouse and Wadhwa, 2013).

These capsulated metals can be incorporated in formulations like tea, soaps, mashed potatoes, etc. Generally, these products are supplied as in powder, and they are water reconstituted and microwave heated by the consumers. Although the use of microwave ovens is increasing both in industry and households, there is little known information on the behavior of metal ions within a gelling matrix submitted to microwaves.

In general, materials such as foods in which microwave energy is dissipated, are generally referred to as lossy materials. Water, the major constituent of foods, is the primary component responsible for dielectric heating. Because of their dipolar nature, water molecules try to follow the applied electric fields as they alternate at very high frequencies; such rotations increase temperature. Besides, ionic conduction could be attributed to salts, composed of positive and negative ions in dissociated form. The net electric field in the oven accelerates the particles and the temperature of them increases, interacting with their neighbors and transfer agitation or

* Corresponding author at: CIDCA (Centro de Investigación y Desarrollo en Criotecología de Alimentos), CCT La Plata, CONICET, Facultad de Ciencias Exactas, UNLP, Calle 47 y 116, La Plata 1900, Argentina. Tel.: +54 2214890741.

E-mail address: lacampa@ing.unlp.edu.ar (L. Campañone).

heat. This heat is then transferred to the other parts of the material (Datta and Anantheswaran, 2005; Datta et al., 2005).

The objectives of this work includes: (i) to investigate the change of the structural properties of beads caused by the thermal process through the FTIR, texture and thermal techniques (DSC); (ii) to compare the behavior of the free (solutions) and encapsulated ions in water solution through the measurement of the temperature increase during microwave heating.

2. Materials and methods

2.1. Preparation of beads

Beads were obtained with a peristaltic pump ((Minipuls 2 Gils, France) by dropping 2% sodium alginate solution (Aldrich, USA) through a syringe into the different gelling solutions. Tested solutions were (0.0055 g/mL) calcium chloride, 0.1 g/mL zinc sulfate heptahydrate (Biopack, Argentina) or an equivolumetric solution of 0.1 g/mL zinc sulfate heptahydrate and 0.1 g/mL ferrous sulfate heptahydrate (Anedra, Argentina). All the beads were maintained in the gelling bath to harden for 15 min. Beads containing, calcium (ACa), zinc (AZn), iron and zinc (AFeZn) were formed. A fraction of the last two types of beads were filtered and dipped in calcium chloride solution (0.0055 g/mL) for 30 min. Beads containing zinc and calcium (AZnCa) and three ions (AZnCaFe) were obtained. Then, beads were washed, filtered and allowed to stabilize in air for 15 min. They were kept at 4 °C for further analysis. Spherical beads were obtained with 4 mm diameter, measured using a Stereo Microscope Leica (Germany). As a summary, four types of capsules were prepared of Calcium Alginate (ACa), Zinc Alginate (AZn), Zinc–Calcium Alginate (AZnCa) and Zinc–Calcium–Iron Alginate (AZnCaFe).

2.2. Determination of bead mineral content

Content of sodium, zinc and iron encapsulated minerals was determined by flame atomic absorption spectrophotometry, according to specifications of the Standard Methods for the examination of water and wastewater APHA (1998) prior to acidic digestion of the samples according to the 25005 Method (AOAC).

2.3. Microwave heating

Water (control) and water containing encapsulated salts were heated in the present work. Also, salt solutions were heated to assess the behavior of the free ions. To compare the temperature increase between bounded and free ions, the same ratio of water/beads or water/solutions (W/W) was used. Two ratios, 15/35 (R1) and 25/25 W/W (R2), were used with a total volume of 50 mL.

A BGH microwave oven with nominal power of 1000 W and 2450 MHz frequency was used to heat the model systems. The heating time was 30 s. Inner temperatures were measured with an optical sensor (Fiso Technol. Inc., Canada) with an acquisition speed of 1 s.

2.4. Fourier Transform Infrared Spectrometry (FTIR)

The analysis was carried out with a Nicolet 380 FTIR spectrometer (USA). Disks were obtained by milling 5 mg of dried beads with 100 mg of KBr and were analyzed by transmission taking 64 scans per experiment with a resolution of 4 cm⁻¹. The analysis was performed on beads with and without microwave heating treatment in duplicate.

2.5. Differential Scanning Calorimetry (DSC)

Thermal analysis was performed on a DSC Q100 (TA Instruments, USA). The equipment was calibrated with the Indium standard. Samples of 15 mg were placed in aluminum capsules hermetically sealed and an empty aluminum capsule was used as the reference. Samples were heated from 20 °C to 290 °C at a scanning rate of 10 °C/min. The analysis was applied to dried beads with and without microwaves heating treatment. Assays were performed in triplicate.

2.6. Texture of beads

A TA.XT 2i texturometer (Stable Micro Systems, UK) was used to obtain the texture profiles (TPA). The analysis consisted of two consecutive cycles of capsule compression (Bourne, 2002). The capsules were placed in Petri dishes with a greater diameter than that of the probe (2.5 cm). The characteristic parameters of the different samples (hardness, cohesiveness and consistency) were obtained from the plot of force as a function of time provided by the equipment. The hardness is defined as the maximum force measured during the first compression, the cohesiveness was estimated as the relationship between the first and the second area obtained by the TPA and the consistency was obtained from the sum of the above mentioned areas.

The tests were conducted in triplicate and the values reported correspond to the average of 10 measurements.

2.7. Statistical analysis

The statistical study of the results was performed using the analysis of variance (ANOVA) with a significance level of 5% or *p*-value <0.05. Mean significant differences were determined using Duncan's multiple comparison test. The statistical analysis was carried out with Systat-software (SYSTAT, Inc., Evanston, IL, USA, 2001) version 10.0.

3. Results and discussion

Previous assays helped select a solution concentration of 0.1 g/mL for zinc sulphate and ferrous sulphate and 2% sodium alginate, based on the integrity and roundness of the beads. Calcium alginate concentration was selected following Anbinder et al. (2011). According to González-Rodríguez et al., 2002 ionic gelation depends on the nature and the ratio of the inorganic ion and the alginate. The authors found differences between the aspect and morphology of Ca²⁺ and Al³⁺ particles, namely that the Al³⁺ particles were disk-shaped with a collapsed center.

In the present work, metal content within the alginate matrix was determined in AZnCaFe beads. Mean values of Zn, Fe and Na (from the alginate salt) were 51.83 g/kg, 43.33 g/kg and 7.20 g/kg, respectively. These results showed that both ions could interact with alginate.

3.1. Microwave heating

In this work, the temperature increase values of salt solutions and encapsulated ions in water (in the same mass ratio: solution or encapsulated ions/water) were compared.

Fig. 1 a and b shows the temperature increase after 30 s of heating for salt solutions and capsules in water (R1 = 15/35), respectively. The different concentrations (R1 or R2) of solutions or capsules did not significantly affect the temperature increase (*p* < 0.05), suggesting that the lower ratio was enough to modify the inner temperature.

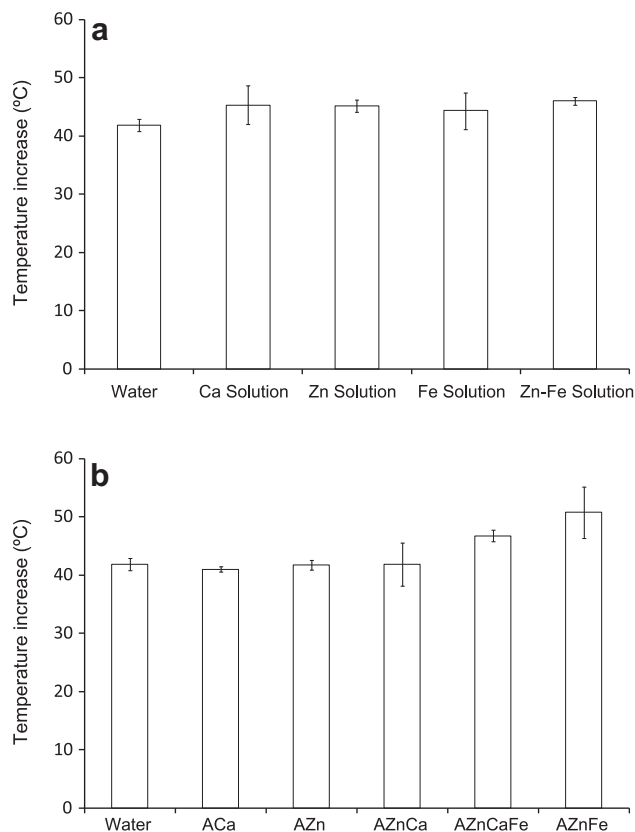


Fig. 1. Temperature increase after 30 s of microwave heating: (a) salt solutions and (b) capsules in water ($R1 = 15/35$).

From the results of temperature increase, no differences in this parameter were found for free in solution or capsulated ions in water ($p < 0.05$). Nevertheless, AZnFe beads in water produced the highest temperature increase. In all cases, the presence of calcium in the beads seemed to decrease the heating rate, defined as the relation between the temperature increase and the heating time (30 s). Carbohydrates do not show appreciable dipolar polarization at microwave frequencies (Datta et al., 2005).

Fisher test showed that the presence of salts increases the rate of heating compared to water ($p < 0.05$). In this sense, Rozzi and Singh (1999) studied the effect of salt content in starch solutions heated with microwaves (5% W/W). They observed there was a significant difference between temperature increase of the suspension with and without salts. The microwave heating of salt solutions at microwave frequencies is attributable to the effects of dipole rotation and ionic charge migration. An increase of heat absorption could be observed, attributable to the last mechanism (Nelson and Datta, 2001).

The presence of the metal ions in the alginate matrix provoked a reduction of the ion movement, but the observed temperature increases were similar to those of the salt solutions. Other effects should be considered to explain this behavior.

Microwave heating of both encapsulated salts in water and emulsion systems could be compared on the basis of their large number of interfaces. According to Barringer et al. (1995), emulsions were heated faster than corresponding layered systems, which in turn were heated faster than a calculated weighted average of individual components. Differences could be attributed to the large number of interfaces occurring in an emulsion or by a single face in layered systems and by a resonant absorption of microwave radiation, which is determined by dielectric properties and the sample size (Samanta et al., 2008). Besides, Barringer et al.

(1995) found those sizes of samples in which the dominant effects were the reflections and the interferences between the waves.

One of the studied systems, the gelled ions in water, has a large interface that may provoke inner reflection of microwaves. According to previous data, several mechanisms acted simultaneously to enhance the heating rates: the interaction of ions with the microwaves, the presence of large number of interfaces and the dielectric properties of the beads, could compensate for the fact that the ions have a reduced mobility.

A texture analysis was also performed on the different type of capsules to determine the effect of microwave heating. ANOVA results indicated that the type of capsule was a significant factor ($p < 0.05$), but not microwave heating treatment for hardness, consistency and cohesiveness parameters. Table 1 shows that AZnCaFe had the highest hardness and consistency. The presence of Ca^{2+} increased hardness and consistency as seen for AZnCa and AZnCaFe.

3.2. Fourier Transform Infrared Spectroscopy (FTIR)

FTIR spectrum of beads (Fig. 2) showed characteristic peaks of alginate: hydroxyl group at $\approx 3440\text{ cm}^{-1}$, carboxylate peaks at ≈ 1625 and 1421 cm^{-1} (asymmetric and symmetric stretching, respectively) and a CH peak at $\approx 2925\text{ cm}^{-1}$.

With regard to the effect of cations, no major differences in band positions were detected between the formed beads, except for asymmetric carbonyl vibration of carboxylate, which showed different values for all capsules. However, it should be taken into account that the peak at 1634 cm^{-1} for AZnCa capsules could be super-imposed with the water vibration (Lawrie et al., 2007). Carbonyl vibration at $\approx 1625\text{ cm}^{-1}$ was considered the most sensitive to the presence of cross-linking agents (Lawrie et al., 2007). Accordingly, Papageorgiou et al. (2010) stated that the frequencies of asymmetric and symmetric carboxylate bands are highly sensitive to the structure of the carboxylate group, the nature of the solvent, the nature of the ligand and the identity of the metal ion. They compared the separation between both carboxylate bands with that of sodium alginate, which is indicative of this type of metal-carboxylate coordination. The difference between asymmetric and symmetric values calculated from Table 2 are above 200 for the three types of beads and higher than the reported values for sodium alginate. This condition corresponded to the unidentate coordination for the central metal atom, characteristic of the egg-box model for alginate gelation (Filipiuk et al., 2005; Papageorgiou et al., 2010). The main differences in FTIR spectra were observed after the addition of Ca^{2+} to already gelled Zn alginate beads. According to Taha et al. (2008), this fact could be attributed to the electrophilic nature of calcium capable of forming electrostatic attractive interactions with algin carboxylates, compared to the softer zinc ions which tend to form covalent-like coordination bonds with carboxylates.

The broad bands in the region $3250\text{--}3440\text{ cm}^{-1}$ indicated the existence of hydroxyl groups involved in the hydrogen bonding of the matrix. These bands became even broader in all the beads after microwave irradiation, which pointed out that hydrogen bonding was enhanced. For this moiety, once again, AZnCa beads

Table 1
Texture parameters of beads after microwave heating.

Parameters	AZn	AZnCa	AZnCaFe
Hardness (N)	3.07 (0.48)	12.05 (0.32)	12.81 (1.14)
Cohesiveness	0.47 (0.02)	9.60 (1.46)	1.20 (0.02)
Consistency	8.45 (1.72)	22.04 (0.95)	46.93 (0.89)

Values between parenthesis correspond to standard deviation.

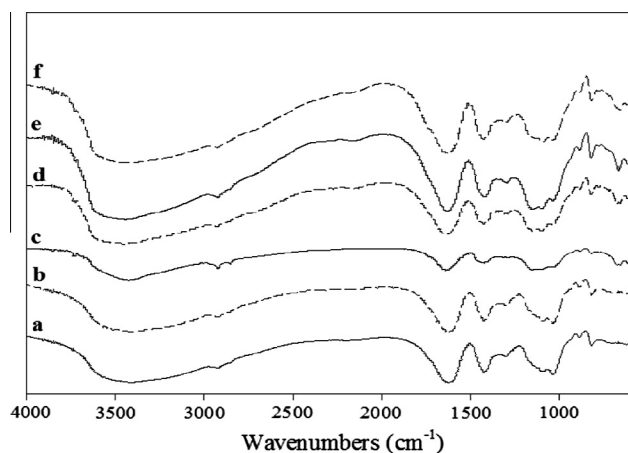


Fig. 2. FTIR spectra of (a) AZn before microwave treatment (MW), (b) AZn after MW, (c) AZnCa before MW, (d) AZnCa after MW, (e) AZnCaFe before MW and (f) AZnCaFe after MW.

were the most affected compared to the other types of beads (Fig. 2).

The peak ascribed to free carboxyl anions at 1738 cm^{-1} reported by Filipiuk et al. (2005) was only visualized for AZnCa beads at 1730 cm^{-1} . Wong et al. (2008) observed that the band assigned to carboxyl moiety at 1726 cm^{-1} was receded upon the transformation of the polymer into the matrix. On this basis, as this peak was not detected for AZnCa beads after microwave treatment, it could be assumed that microwave reinforced matrix interaction. Similarly, after the treatment, the band at 2851 cm^{-1} of AZnCa capsules was not observed, probably indicating a higher interaction of polymer chains matrix via CH moiety. Other reports, dealing with microwave heating, indicated that the drying of alginate and pectinate beads under different irradiation conditions led to crosslinking and even breakdown of polymer chains (Wong et al., 2002; Wong and Nurjaya, 2008). In the present work, in spite of the increased extent of polymer interaction demonstrated by microwave drying (Wong et al., 2005), only slight modifications on structure of the beads were detected by FTIR because the beads remained wet before and after microwave treatment.

3.3. Differential Scanning Calorimetry (DSC)

Fig. 3 shows DSC thermograms of capsules before and after microwave treatment. Before microwave treatment, the endothermic peak at 181 °C of capsules of AZn shifted to 177.5 °C when calcium was incorporated to the Zn alginate matrix. Another small peak at 213.7 °C was observed for AZnCa capsules. Similar values were previously reported for calcium alginate (Wong et al., 2002; Anbinder et al., 2011). Differences in the peak temperature can

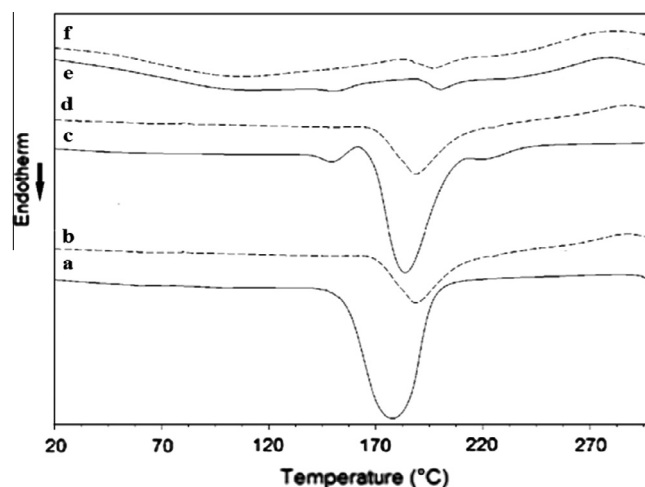


Fig. 3. DSC thermograms of (a) AZn before microwave treatment (MW), (b) AZn after MW, (c) AZnCa before MW, (d) AZnCa after MW, (e) AZnCaFe before MW and (f) AZnCaFe after MW.

be related to changes in the mechanism of the cation bonding. Calcium-carboxylate bonds are mainly of ionic nature while zinc-carboxylate counterparts have a coordinate character (Aslani and Kennedy, 1996; Taha et al., 2008). Also, since calcium and zinc are divalent cations, their bonding to alginate was expected to occur in a planar two-dimensional manner as represented in the egg-box model. In the case of AZnCa, it could be assumed that a mix-gel was formed where both types of bindings are present in the same matrix.

With regard to incorporation of a third ion, in the present work it should be taken into account that Fe^{2+} is easily oxidized to Fe^{3+} , the trivalent iron could be expected to form a three dimensional bonding structure with the alginate (Olukman et al., 2012). Accordingly, Fig. 3 shows more complex thermograms for AZnCaFe beads. The broad peak centered at 100 °C is commonly attributed to bead dehydration (Smitha et al., 2005).

After microwave heating, peak temperature of treated capsules shifted to higher values compared to the capsules before microwave heating. This fact could be related to the increase in hydrogen bindings within the alginate matrix due to the microwave treatment.

4. Conclusions

The experimental results of temperature increase show that the presence of Zinc and Iron increased inner temperature (beads in water and free in solutions) of the system with respect to water. Texture analysis indicated that the presence of calcium increased the hardness and consistency of the beads.

Table 2

Assignment of the main vibrational bands for capsules of Zn, ZnCa and ZnCaFe alginate.

Assignments	AZn		AZnCa		AZnCaFe	
	Before ^a (cm^{-1})	After (cm^{-1})	Before (cm^{-1})	After (cm^{-1})	Before (cm^{-1})	After (cm^{-1})
—OH	3411	3403.4	3444	3452	3440.1	3432
—CH	2925.3	2921	2921.2	2921.2	2929.4	2929.4
—CH	—	—	2851.7	—	—	—
C=O of COOH	—	—	1730	—	—	—
COO ⁻ asymmetric	1621	1621	1634.3	1638.1	1625	1625.8
COO ⁻ symmetric	1421	1421.5	1421	1425.6	1421	1425.6
C—O	1298.9	1298	1298.9	1307.1	1298	1298.9

^a Indicates the conditions of the assayed capsules: before or after microwave heating.

Calcium ion behavior can be explained on the basis of its strong interaction with the polymer chains that imparted a different microstructure as compared to the zinc alginate formulation. This observation could be inferred from the DSC and the FTIR analysis.

The presence of iron in the AZnCaFe beads even showed a more complex structure as revealed by DSC thermogram and texture parameters.

The incorporation of capsulated ion beads in foods is currently under experimental study at our laboratory. The encapsulated ions may be incorporated to enrich the nutritive value of food products masking the metallic taste and accelerating microwave heating.

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References

- Anbinder, P.S., Deladino, L., Navarro, A.S., Amalvy, J.I., Martino, M.N., 2011. Yerba mate extract encapsulation with alginate and chitosan systems: interactions between active compound encapsulation polymers. *J. Encapsul. Adsorpt. Sci.* 1, 80–87.
- Aslani, P., Kennedy, R.A., 1996. Studies on diffusion in alginate gels. I. Effect of cross-linking with calcium or zinc ions on diffusion of acetaminophen. *J. Controlled Release* 42, 75–82.
- Barringer, S.A., Davis, E.A., Gordon, J., Ayappa, K.G., Davis, H.T., 1995. Power absorption during microwave heating of emulsions and layered systems. *J. Food Sci.* 60 (5), 1132–1136.
- Bourne, M.C., 2002. *Food Texture and Viscosity: Concept and Measurement*, second ed. Academic Press, NY, New York.
- Datta, A.K., Anantheswaran, C.R., 2005. *Handbook of Microwave Technology for Food Applications*. Marcel Dekker, New York.
- Datta, A.K., Sumnu, G., Raghavan, G.S.V., 2005. Dielectric properties of foods. In: Rao, M.A., Rizvi, S.S.H., Datta, A.K. (Eds.), *Engineering Properties of Foods*, third ed. CRC Press Taylor & Francis Group, Boca Raton.
- Deladino, L., Anbinder, P.S., Navarro, A.S., Martino, M.N., 2008. Encapsulation of natural antioxidants extracted from *ilex paraguariensis*. *Carbohydr. Polym.* 71, 126–134.
- Desai, K.G.H., Jin Park, H., 2005. Recent developments in microencapsulation of food ingredients. *Drying Technol.* 23 (7), 1361–1394.
- Filipiuk, D., Fuks, L., Majdan, M., 2005. Transition metal complexes with uronic acids. *J. Mol. Struct.*, 705–709.
- González-Rodríguez, M.L., Holgado, M.A., Sanchez-Lafuente, C., Rabasco, A.M., Fini, A., 2002. Alginate/chitosan particulate systems for sodium diclofenac release. *Int. J. Pharm.* 232, 225–234.
- Gouin, S., 2004. Microencapsulation: industrial appraisal of existing technologies and trends. *Trends Food Sci. Technol.* 15 (7–8), 330–347.
- Lawrie, G., Keen, I., Drew, B., Chandler Temple, A., Rintoul, L., Fredericks, P., Grondahl, L., 2007. Interactions between alginate and chitosan biopolymers characterized using FTIR and XPS. *Biomacromolecules* 8, 2533–2541.
- Nelson, S.O., Datta, A.K., 2001. Dielectric properties of food materials and electric field interactions. In: Datta, A.K., Anantheswaran, R.C. (Eds.), *Handbook of Microwave Technology for Food Applications*. Marcel Dekker, New York, USA.
- Olukman, M., Şanh, O., Solak, E.K., 2012. Release of anticancer drug 5-fluorouracil from different ionically crosslinked alginate beads. *J. Biomater. Nanobiotechnol.* 3, 469–479.
- Papageorgiou, S.K., Kouvelos, E.P., Favvas, E.P., Sapalidis, A.A., Romanos, G.E., Katsaros, F.K., 2010. Metal-carboxylate interactions in metal-alginate complexes studied with FTIR spectroscopy. *Carbohydr. Res.* 345, 469–473.
- Sahidi, F., Han, X., 1993. Encapsulation of food ingredients. *Crit. Rev. Food Sci. Nutr.* 33 (6), 501–547.
- Samanta, S.K., Basak, T., Sengupta, B., 2008. Theoretical analysis on microwave heating of oil-water emulsions supported on ceramic, metallic or composite plates. *Int. J. Heat Mass Transfer* 51, 6136–6156.
- Sarubin Fragaakis, A., Thomson, C., 2007. *The Health Professional's Guide to Popular Dietary Supplements*, third ed. American Dietetic Association, USA.
- Smitha, B., Sridhar, S., Khan, A.A., 2005. Chitosan-sodium alginate polyion complexes as fuel cell membranes. *Eur. Polym. J.* 41, 1859–1866.
- Rozzi, N.L., Singh, R.K., 1999. The effect of selected salts on the microwave heating of starch solutions. *J. Food Process. Preserv.* 24, 265–273.
- Sun-Waterhouse, D., Wadhwa, S., 2013. Industry-relevant approaches for minimising the bitterness of bioactive compounds in functional foods: a review. *Food Bioprocess Technol.* 6 (3), 607–627.
- Taha, O.M., Nasser, W., Ardakani, A., Alkhatib, H.S., 2008. Sodium lauryl sulfate impedes drug release from zinc-crosslinked alginate beads: switching from enteric coating release into biphasic profiles. *Int. J. Pharm.* 350, 291–300.
- Tannenbaum, S.R., Young, V.R., 2005. *Vitamins and minerals*. In: Fennema, O.R. (Ed.), *Food Chemistry*, second ed. Marcel Dekker, New York, USA, pp. 477–544.
- Wong, T.W., Chan, L.W., Kho, S.B., Heng, P.W.S., 2002. Design of controlled release solid dosage forms of alginate and chitosan using microwaves. *J. Controlled Release* 84, 99–114.
- Wong, T.W., Chan, L.W., Kho, S.B., Sia Heng, P.W., 2005. Aging and microwave effects on alginate-chitosan matrices. *J. Controlled Release* 104, 461–475.
- Wong, T.W., Wahab, S., Anthony, Y., 2008. Drug release responses of zinc ion crosslinked poly (methyl vinyl ether-co-maleic acid) matrix towards microwave. *Int. J. Pharm.* 357, 154–163.
- Wong, T.W., Nurjaya, S., 2008. Drug release property of chitosan pectinate beads and its changes under the influence of microwave. *Eur. J. Pharm.* 69, 176–188.