Slow Release Polymer–Iodine Tablets for Disinfection of Untreated Surface Water

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ABSTRACT: Simple water treatment devices are designed to treat small amounts of drinking water for home use. This study was undertaken to develop an iodine-releasing polymeric formulation and examine its potential as a domestic water purifier for untreated surface water. The antimicrobial tablet formulation was made from gum arabic (GA), poly(vinylalcohol) (PVA), ethyl cellulose (EC), and poly(vinylpyrrolidone)-iodine (PVP-I). The formulation consisted of a dispersible core tablet surrounded by a hydrophilic coating of EC and poly(ethylene glycol) mixture. These stable, non-vaporizing, and water-insoluble tablets slowly release iodine through diffusion over 48 h when suspended in water. The swelling behavior and release were observed to be the functions of excipient composition, iodine loading, and coating materials. Iodine release was determined by UV–VIS spectroscopy and volumetric titrations. The tablets were also assessed for antimicrobial activity against *Escherichia coli, Staphylococcus aureus, Listeria monocytogenes Scott A*, and *Salmonella typhimurium.* The disinfection efficiency of the developed tablets was compared with a commercial formulation (Potable Aqua®) as both contain iodine-releasing active compounds and work on the antimicrobial property of released iodine. The difference between the two formulations is that water-dispersible Potable Aqua® has a higher amount of free iodine quickly available in water thereby making it a fast-action emergency water purifier, whereas the developed water-insoluble polymer–iodine tablets act slowly and require 24 h to show the same disinfection efficacy with lower content of iodine in water. Overnight release of iodine in water from polymer–iodine tablets was effective in 99.9% reduction of an initial cell count of $\sim 10^7$ colony forming units (cfu)/mL. © 2010 Wiley Periodicals, Inc. J Appl Polym Sci 117: 329–334, 2010

Key words: iodine-releasing polymer; slow-release tablet; water disinfectant; antimicrobial polymer

INTRODUCTION

Water quality of untreated surface water consumed by people in underdeveloped regions of the world is a primary health and safety concern for all. Small-scale water treatment systems are good alternatives to piped water supply and treatment plants that are not possible in remote areas of many developing countries. An urgent need exists to introduce simple, inexpensive, and appropriate water purification methods.[1,2] One such system could be an in-house water treatment device based on insoluble iodinated polymeric disinfectants.

The history of iodine as a water disinfectant goes back to World War I when French troops used iodine for water treatment.[3] The US army in World War II used tetraglycine hydroperiodide (TGHP) for the same purpose[4]; TGHP is still used as water purifying tablets under the brand name of Potable Aqua®. A review[5] of the human trials on the safety of iodine ingestion indicates that neither the maximum recommended dietary dose (2 mg/day) nor the maximum recommended duration of use (3 weeks) has a firm basis for determining the threshold level of iodine intake that affects thyroid function. A study-based report[6] from WHO mentions that <10% of general population responds adversely to excess iodine. NASA has used iodine as a biocidal agent in spacecraft water systems for Apollo missions[7] and is currently using an iodinated ion-exchange resin that releases iodine into the water stored in tanks in the International Space Stations.[8,9] In addition, reports and patents are available on disinfection of drinking water by various iodine formulations.[10–12] Among these, several iodine-release systems have been prepared for water disinfection by incorporating elemental iodine into synthetic polymers; however, few reports use poly (vinylpyrrolidone)-iodine (PVP-I) as the matrix-bound disinfecting agent for such purpose. Iodine is said to be "tamed" when bonded to PVP as several drawbacks associated with the use of elemental

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iodine, such as, high toxicity, high level of irritation, and staining power are considerably reduced.[13] Reports[14,15] are available on the development of bioadhesive and sustained release of vaginal tablets and dental implants for treating peridontitis based on PVP-I incorporated formulations. More recently, PVP-I was blended with an aqueous solution of gum arabic (GA) and poly(vinylalcohol) (PVA) to prepare a crosslinked hydrogel film for iodine delivery.[16]

The aim of this study was to examine the home use of PVP-I incorporated tablet formulations made from GA, PVA, and ethyl cellulose (EC) for water purification. The membrane-coated slow-release iodine tablet (P-I) was characterized and evaluated for antimicrobial activity against various bacterial strains including common harmful bacteria, such as, *Staphylococcus aureus* and *Escherichia coli*. The performance of the tablet was also compared with a marketed formulation, Potable Aqua® (P-A) containing TGHP as the active agent.

MATERIALS AND METHODS

Reagent-grade GA, PVA (98–99% hydrolyzed, M_w 31,000–50,000), EC (ethoxy content 48%), PVP-iodine complex, poly(ethylene glycol) (PEG) (M_n 600), carbon tetrachloride, potassium iodide, volumetric standard sodium thiosulphate 0.1*N* solution in H_2O, iodine volumetric standard 0.1*N* solution (consisting of 5–9% I_2 and 10–20% potassium iodide dissolved in water and stabilized by hydrochloric acid), potassium dichromate, and soluble starch were purchased from Sigma-Aldrich (St. Louis, MO). Commercial Potable Aqua® tablets are manufactured by Wisconsin Pharmacal Company (Jackson, WI).

For the microbiological studies, trypticase soy broth, nutrient agar, and bacto peptone were purchased from Difco Laboratories (Sparks, MD). The bacterial strains of *E. coli* (Top 10), *Staph. aureus* (ATCC 25973), *Listeria monocytogenes Scott A*, and *Salmonella typhimurium* were obtained from Prof. M.L. Chikindas (Food Science Department, Rutgers University, New Brunswick, NJ). The initial cell count of the microorganisms (in cfu/mL) cultured for assessment of antimicrobial activity is as follows:

E. coli $= 5.6 \times 10^6$, *Staph. aureus* $= 4.1 \times 10^5$,
S. typhimurium $= 1.4 \times 10^7$, and
Listeria monocytogenes Scott A $= 2.4 \times 10^7$.

Preparation of polymer–iodine tablets

The tablets were prepared with a fixed weight of PVP-I powder in each sample and the excipients varied to optimize the water resistance and release of iodine. The ingredients were mixed well using a mortar and pestle. The mixture (500 mg) was compressed in a laboratory Carver Press (Carver, Wabash, IN) under 10,000 pounds for 5 min using a 13 mm stainless steel disk mold. The tablets were weighed and their diameter, height, and density were determined. Samples were stored at 50°C for a week to increase the ingredient compatibility and allow the free iodine of PVP-I to interact with the hydroxy-polymers.[16] Finally, the tablets were dip-coated in a mixture of EC and PEG dissolved in carbon tetrachloride (3.75/5% w/v) and then dried at 50°C for about a week to constant weight. The samples with similar weight gain were chosen for swelling and release studies.

Tablet characterization

Physical characteristics

The height (h) and diameter (d) of the tablets were measured with a vernier caliper and the density calculated using the formula: density $= m/(h \times 7.85 \times 10^{-1} d^2)$. The values were averaged from five tablets per series.

Swelling studies

To study swelling behavior of the tablets in water and gravimetrically measure their water absorbance, the dry and weighed tablets ($h = 0.38 \pm 0.01$ cm; $d = 1.30 \pm 0.01$ cm; and $\rho = 1.10 \pm 0.20$ g/cc) were immersed in 20 mL distilled water at room temperature. The samples were removed at different time intervals (1/2, 1, 2, 3, 4, 6, 8, 24, and 48 h), weighed after quickly blotting the excess water from their surface with filter paper and quickly returned to the media. Percent water absorption was calculated using eq. (1):

$$\text{Percent swelling} = [(W_s - W_d)/W_d] \times 100 \quad (1)$$

W_s and W_d are the weight of the tablets in swollen and dry states, respectively. The swelling studies were performed in triplicate.

Release studies

Several stock solutions were prepared: (i) 0.02 g/mL iodine solution was prepared by mixing 16.4 mL iodine volumetric standard and water to a final volume of 100 mL; (ii) aqueous solution of PVP-I (0.01×10^{-1} g/mL); and (iii) aqueous solution of KI (3.03×10^{-4} g/mL). The UV–VIS spectra were recorded in a spectrophotometer (Beckman DU 520) to identify the peak intensity and λ_{max} values of different prominent forms of iodine, such as, I^-, I_3^-, and I_2. Lambert-Beer curves were plotted using several dilute solutions prepared from the stock solutions. Different iodine species released from the developed GA/PVA/EC/PVP-I tablets into water were observed by monitoring peaks from 200 to 600 nm.

The release was monitored in 10 mL water that was replaced with fresh water at frequent intervals. Release of iodine into water from a "control" formulation containing the same weight of PVP-I without excipients was also studied.

Estimation of available iodine

PVP-I is a complex that contains 9–12% of available iodine as estimated by titrimetric method.[17] The method involves titration of aqueous PVP-I solution against a standardized sodium thiosulphate solution using starch as indicator. PVP-I powder (150 mg) was dissolved in 100 mL water and titrated immediately with 0.02*N* sodium thiosulphate solution, freshly prepared and standardized with potassium dichromate solution. One Potable Aqua® tablet containing TGHP, $4[(NH_2CH_2CO_2H)_2HI]$. $5I_2$ as the active agent (weight 118 mg) was dissolved in 100 mL water and similarly titrated to determine the content of available iodine per tablet. The amount of available iodine in 100 mL water released from a coated polymer–iodine tablet was similarly estimated.

Assessment of antimicrobial activity

The efficacy of the polymer–iodine tablet (P-I) as a bactericide was evaluated along with the "control" formulation without PVP-I (C) and commercial water-dispersible Potable Aqua® (P-A) tablet containing TGHP against *E. coli, Staph. aureus, Listeria monocytogenes Scott A*, and *S. typhimurium.*

The bacterial cells were grown overnight in TS broth after inoculating one colony from a fresh plate of the microorganism on day 1. On day 2, 1% of the cell suspension was transferred to a 25 mL tube containing sterile TS broth and incubated overnight. On the day of the experiment (day 3), 100 mL sterile distilled water in a conical flask was inoculated with 1 mL suspension to cell density of $\sim 10^7$ cfu/mL. The actual density of the bacterium in the flask at time $t = 0$ was determined by standard plate count (SPC) method[18] and as reported in Materials and Methods section. Four other conical flasks (each of them containing 100 mL sterile water) were similarly inoculated with 1 mL cell suspension. The samples (P-I, P-A, and control) were then added to the flasks; one without a sample was used as a control to enumerate the number of viable cells in the flask at $t = 24$ h. All four flasks were placed in a shaker at room temperature.

At 1 h, 1 mL water sample was withdrawn from the flasks and serially diluted into tubes containing sterile buffer solution. Two samples of 100 μL from each dilution were plated onto nutrient agar plates. The plates were incubated for 24–48 h. The colonies for each dilution were counted using a colony counter and averaged and the average number was used to calculate the cell density in cfu/mL.

At 24 h, the number of viable cells was determined by SPC method as mentioned earlier. This experiment was repeated by suspending one P-I tablet overnight in 100 mL water inoculated with 10^6 to 10^7 cells/mL. Another flask with 100 mL water containing no tablet was similarly inoculated and used as control. After 24 h, the bacterial cell density in both the flasks was determined by the SPC method. Data reported are the mean of values ± 0.12 SD obtained from triplicate experiments.

RESULTS AND DISCUSSION

PVP-I incorporated and hydrophilic membrane-coated polymer tablets were developed to disinfect contaminated surface water by a slow release of iodine. Various compositions were evaluated for desirable physical properties including swelling and release rates for the formulations. Table I presents the composition of the tablet formulations selected and tested. The coated tablets were stored at 50°C for about a week to evaporate the coating solvent and stabilize the weight. The weight gain by the tablets after coating was ~ 3%.

The swelling behavior of the tablets was studied to determine the percent water absorption values with changing iodine loading, the ratio of hydrophilic to hydrophobic excipients, and composition of the coating mixture. The results of swelling studies are presented in Figures 1 and 2.

The samples containing 40% PVP-I (S-series) showed high degree of swelling in water than those

TABLE I
Compositions of the Polymer–Iodine Tablet Formulations

Formulation codes	Ingredients (wt %)			
	PVP-I	GA	PVA	EC
C1	40	0	0	60
C2	0	40	30	30
C3	30	0	0	70
C4[a]	100	0	0	0
S1	40	15	15	30
S2	40	20	15	25
S3	40	20	20	20
S4	40	30	20	10
T1	30	8	12	50
T2	30	16	14	40
T3	30	20	20	30
T4	30	40	20	10
T5[a]	30	16	14	40
T6[a]	30	8	12	50

C-series (controls); S- and T-series contain 40% and 30% PVP-I, respectively.
[a] Samples coated with EC/PEG.

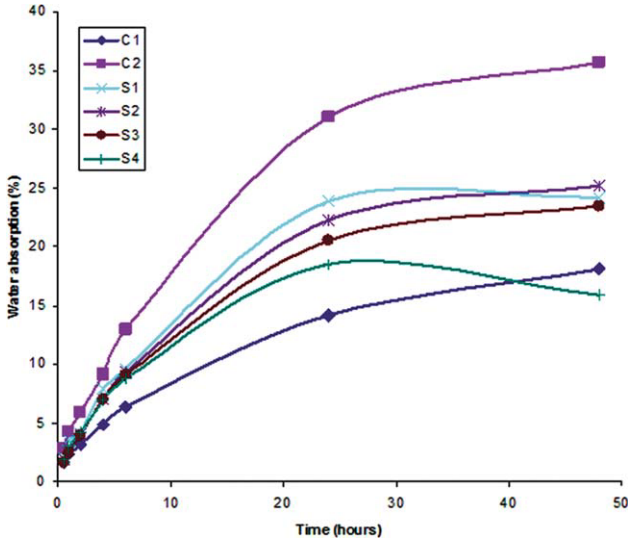

Figure 1 Percent water absorption by polymer–iodine tablets containing 40% PVP-I and control formulations. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

containing 30% PVP-I (T-series). Also, tablets containing higher amount of PVP-I (S-series) could not sustain their firm shape in water after 48 h of swelling study, whereas the tablets containing 30% PVP-I (T-series) retained their stability in water for a week. The degree of swelling decreased as the amount of EC per tablet increased and the matrix became more hydrophobic. The samples C1 (40% PVP-I/60% EC) and C3 (30% PVP-I/70% EC) showed the lowest degree of swelling. Based on the results of the swelling studies, tablets containing 30% PVP-I were chosen for quantitative release studies. To have desirable water absorption capacity and facilitate diffusion-induced slow release of iodine, the tablets were coated with EC/PEG solution in carbon tetrachloride. PEG was selected as the plasticizer because it is soluble in CCl_4 and has been reported to be used with EC for coating pharmaceuticals.[19] Figure 2 compares the swelling behavior of tablets coated with EC and EC/PEG; samples coated with EC/PEG absorbed a high content of water.

The amount of iodine released in water from the tablets was measured quantitatively by UV–VIS spectroscopic and titrimetric methods. Both methods have limitations: iodine undergoes multiple reactions in water giving rise to various concentrations of different iodine-containing species in solution.[9] Thus, the spectroscopic method may not be very accurate to estimate all the species due to spectral interferences[20] and titrimetric method cannot be used for the release of very small amount of iodine in water.[14] The interaction of iodine with PVP to form PVP-I complex is somewhat controversial further complicating the study of release of the iodine from the complex.[9,21,22]

Figures 3 and 4 present and compare the UV–VIS spectra of standard solutions of iodine (consisting of I_2 and KI dissolved in water), PVP-I, KI, released iodine species in water from polymer–iodine tablets, the control formulation (consisting of 100% PVP-I), and Potable Aqua® tablet. The scan of iodine solution shows clear peaks for I_3^- (288 and 351 nm) and I^- (225 nm) as reported.[9] I^- peak at 225 nm is the only one also present in the spectrum of KI. The predominant iodine species present in water when PVP-I and Potable Aqua® tablets are dissolved in water should be I_3^-, I_2, I^-, and HOI according to the hydrolysis reactions of iodine[7,9]:

$$I_2 + H_2O = HOI + I^- + H^+$$

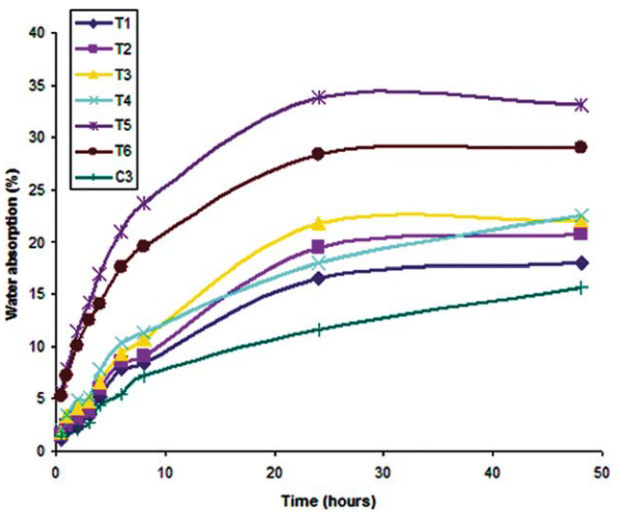

Figure 2 Percent water absorption by polymer–iodine tablets containing 30% PVP-I and control formulations. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

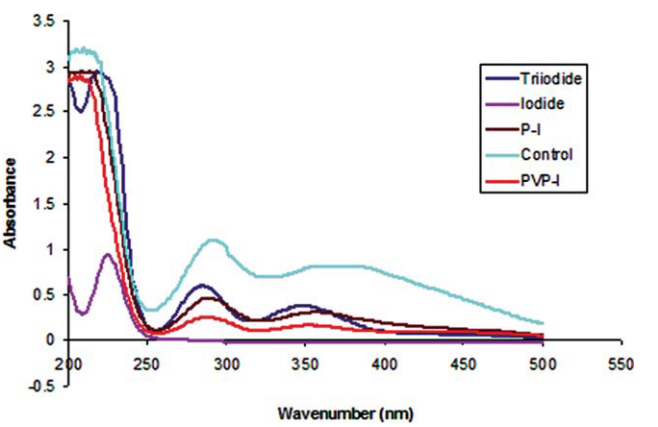

Figure 3 UV–VIS spectra of standard solutions of iodine, PVP-I, KI, and released iodine in water from P-I tablets and control (100% PVP-I). [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

$$I_2 + I^- = I_3^-$$

However, because of spectral interference[20] and usual weak intensity peak of I_2,[12] only two distinct peaks (288 and 351 nm for I_3^-) could be identified in PVP-I (Fig. 4). The I^- peak at 225 nm could not be detected in PVP-I, released iodine from the "control" and P-I tablet formulations; the peak at 351 nm shifts and appears as a broad peak ranging from 362 to 365 nm probably due to the formation of I_5^- ($I_3^- + I_2 = I_5^-$).[7] The proposed structure of PVP-I in the literature includes a proton coordinated between two carbonyl groups and possible involvements of I_2, I_3^-, and I_5^- with PVP[23] (Fig. 5). Of two absorbance maxima at λ_{288} and λ_{351} recorded for PVP-I, a shift occurred in the λ_{max} value of the second peak for PVP-I in the presence of excipients and iodine release from the tablets was measured at 288 nm. Both wavelengths have been reported to be used for estimation of PVP-I.[24] It was noted that per hour release of iodine was initially very slow and an insignificant amount (<0.05 μg/mL) was released by 6 h. An overnight suspension of the tablet in water seemed more appropriate to measure per day release of iodine and more relevant to its use. The amount of I_3^- present in water sample obtained from a P-I tablet in 2 days was calculated to be as 0.28 mg/mL. Titrimetric method[17] was used to determine the amount of available iodine (iodine titratable with sodium thiosulphate) released from PVP-I containing tablets in 24 h and was compared with the amount

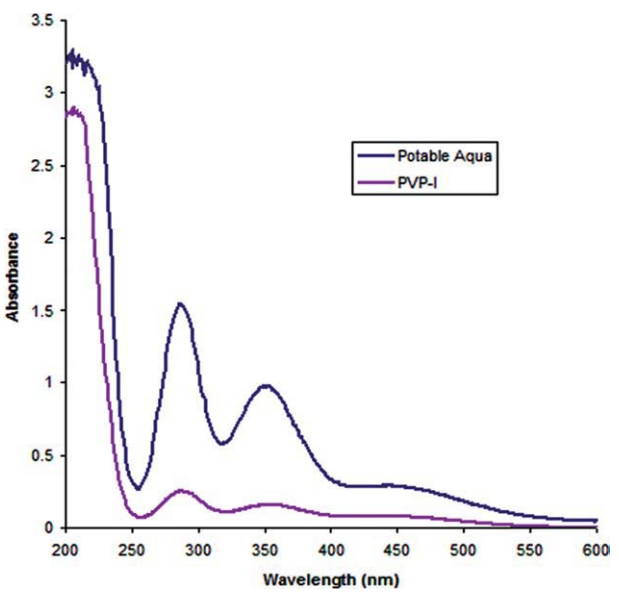

Figure 4 UV–VIS spectra of TGHP in Potable Aqua® tablet and PVP-I powder showing peaks at 288 nm, 351 nm (I_3^-), and 460 nm (I_2). [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

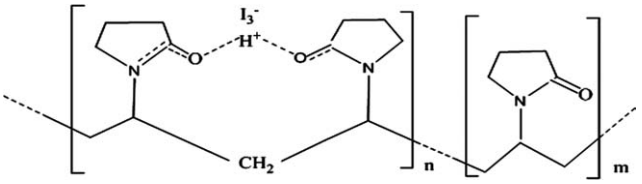

Figure 5 Structure of poly(vinylpyrrolidone)-iodine ($n : m = 1 : 18$).

available instantaneously from an equivalent amount of PVP-I used in the formulation and the commercial Potable Aqua® tablet. The amount of available iodine from PVP-I and a Potable Aqua® tablet was calculated to be 10.2% and 7.55 %, respectively, and is comparable to the label. Available iodine in water released from a P-I tablet containing 30% PVP-I in 24 and 48 h measured similarly were estimated to be 1.64 mg/mL and 3.83 mg/mL, respectively. Similar conditions were maintained when the tablets were evaluated for antimicrobial activity to determine if 24 h release of iodine from a P-I tablet is sufficient to disinfect contaminated water.

There was no significant change in the number of bacterial cells suspended for 24 h in sterile water containing no sample. Because P-I tablets were found to slowly release iodine and bactericidal concentration of iodine was not sufficiently released within a few hours to inactivate the microorganisms, the antimicrobial experiments were recalibrated to evaluate their antimicrobial activity over 24 h. Overnight release of iodine from the tablets could kill the bacteria 99.9% effectively and no colony growth was observed in the plates inoculated with cells that were in contact with the tablets. The plates, however, showed growth when inoculated with cells kept in contact with "control" tablets containing 0% PVP-I for the same contact period. In contrast to our proposed formulation, the commercial tablet (Potable Aqua®) could inactivate the cells in 1 h. P-A is water-dispersible and thus has a high amount of free iodine quickly available in water. As a result, 99.9% killing of initial bacterial cells was achieved in 1 h. In comparison, P-I was slower in action, but showed the same disinfection efficiency with a lower iodine content which gave it an advantage over P-A.

CONCLUSIONS

An iodine based water disinfectant was prepared to avoid the drawbacks associated with using elemental iodine as the biocidal agent. The tablet formulation works on a simple slow-release technology and is meant for people who need to purify stored untreated surface water for drinking purpose. These water-insoluble coated polymer–iodine tablets

slowly release iodine and inactivate the microorganisms. The tablet formulation showed significant bactericidal activity against four representative bacterial strains. Although the contact time required by the proposed formulation for 99% reduction is longer compared with the commercial formulation, the developed water purifier would have advantages in terms of cost and residual iodine content in water.

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References

1. Dietvorst, C. Household Water Treatment [FAQ sheet]; IRC International Water and Sanitation Center: Delft, The Netherlands, 2007.
2. Choudhury, M.; Sattar, S. A. In Domestic Water Treatment for Developing Countries, Drinking Water Microbiology; McFeters, G. A., Ed.; Springer-Verlag: New York, 1990; p 168.
3. White, G. C. The Handbook of Chlorination and Alternative Disinfectants, 3rd ed.; Van Nostrand Reinhold Publishing: New York, 1992.
4. Morris, J. C.; Chang, S. L.; Fair, G. M.; Contant, G. H. Ind Eng Chem 1953, 45, 1013.
5. Backer, H.; Hollowell, J. Environ Health Perspect 2000, 108, 1679.
6. WHO. 661, Iodine [WHO Food Additives Series 24]; WHO: Geneva.
7. Atwater, J. E.; Richard, L. S.; Schultz, J. R. J Environ Sci Health Part A 1996, 31, 1965.
8. Atwater, J. E.; Wheeler, R. R., Jr.; Sauer, R. L.; Schultz, J. R. SAE Technical Paper Series No. 932175; SAE International: Warrendale, PA, 1993.
9. Gazda, D. B.; Lipert, R. J.; Fritz J. S.; Porter M. D. Anal Chim Acta 2004, 510, 241.
10. Marchin, G.; Fina, L. Crit Rev Environ Control 1989, 19, 277.
11. Belfer, W. A.; Petillo, P. J. U.S. Pat. 6,106,854 (2000).
12. Punyani, S.; Narayanan, P.; Vasudevan, P.; Singh, H. J Appl Polym Sci 2007, 103, 3334.
13. Siggia, S. J Am Pharm Assoc 1957, 46, 201.
14. Garg, S.; Jambu, L.; Vermani, K. Drug Dev Ind Pharm 2007, 33, 1340.
15. David, A. T.; Kurien, S.; Udupa, N.; Verma, B. R. Indian J Dent Res 1994, 5, 101.
16. Mazumdar, N. A.; Abid, Z.; Ahmed, I.; Hasan, N. J Appl Polym Sci 2008, 109, 775.
17. United States Pharmacopeial Convention, Inc. The US Pharmacopeia, Vol. XXVII; United States Pharmacopeial Convention, Inc.: Rockville, MD, 2004.
18. Davis, D., Ed. General Microbiology Laboratory Manual 680; Department of Biochemistry and Microbiology, Rutgers University: New Brunswick, NJ, 2008, p 3901.
19. Rowe, R. C.; Sheskey, P. J.; Owen, S. C. Handbook of Pharmaceutical Excipients, 5th ed.; Pharmaceutical Press: London, 2006.
20. Oster, G.; Immergut, E. H. J Am Chem Soc 1954, 76, 1393.
21. Pandeeswaran, M.; Elango, K. P. Spectrochim Acta Part A 2009, 72: 789.
22. Guzenko, N. V.; Voronina, O. E.; Vlasova, N. N.; Voronin, E. F. J Appl Spectrosc 2004, 71, 151.
23. Schenck, H. U.; Simak, P.; Haedicke, E. J Pharm Sci 1979, 68, 1505.
24. Adham, I. S.; Gilbert, P. Int J Pharm 1986, 34, 45.