



Kinetics of periodate oxidation of polyoxyethylene – 300, a biodegradable pharmaceutical polymer

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ABSTRACT

Polyoxyethylene – 300 (POE) is a well-known biodegradable pharmaceutical polymer. In order to understand the stability of POE and to derive the reaction rate law, the title reaction was carried out in aqueous alkaline medium. Reaction was found to be first order dependent on the concentration oxidant (periodate) and independent of substrate (POE) concentration. A retardation of reaction rate with an increase in hydroxide concentration shows an inverse fractional order in it. Based on the studies of the temperature dependence of reaction, evaluated the activation parameters.

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INTRODUCTION

Poly oxyethylene (POE) is a freely obtainable polymer in an array of molecular weights. A variety of POEs exhibit solubility in water and some of the organic solvents. The other name is PEG (poly ethylene glycol) when its molecular weight is less than one lakh. PEGs (having a molecular weight less than a thousand) are colorless and viscous liquids (Baily and Koleske, 1976). Polyethylene glycols (PEGs) are well-known excipients (Debotton and Dahan, 2017). In controlled drug delivery, PEG copolymers with polylactic acid (PLA) are used (Xu et al., 2019). Protein-based medications accumulate the protein

deposits in the blood, which can be reduced by opting PEG surface coating on them (Antwerp et al., 2002). Osmotic action of PEG supports its usage as a laxative (Savino et al., 2012). Liquid PEGs (200 - 600) are used in pharmaceutical preparations of oral and intravenous administration (D'souza and Shegokar, 2016). As antidotes, they remove the toxic substances from the surface of burned skin (Cartotto et al., 1996).

In addition, a spectrum of industrial applications is shown by PEGs. In view of low toxicity, cheap cost, biodegradability and ready availability, PEGs possess high advantage for solvents (Zhang et al., 2004). In addition, PEG is a well-known phase transfer catalyst (Xie et al., 2000) and reducing agent in organic synthesis in the presence of microwave irradiation (Bendale and Khadiilkar, 2000; Sauvagnat et al., 2000). Chromeno[3,4-*b*]quinoline derivatives were synthesized efficiently in a "green" solvent like PEG 300 using Cu(II)BHPPDAH complex as heterogeneous catalyst (Sharghi et al., 2013). In most of the cross-coupling reactions, PEGs are used as effective green solvents (Razler et al., 2009). PEG-300 was proved to be an excellent medium to result in high yields of the biaryl nucleus in a cross-coupling of aryl chlorides and phenylboronic acids through Suzuki-

Miyaura cross-coupling (Yin *et al.*, 2006). Under thermal conditions, high yields (98%) of 1-iodo-4-nitrobenzene and phenylboronic acid were obtained by carrying out Suzuki cross-coupling reactions in PEG-300 (Silva, 2010). Dziurka (2005) included PEG 300 in resin mixture and studied its influence on the properties of PMDI resin. PEG is also used as a solvent in the preparation of inorganic nano-materials like TiO₂ nanoparticles in a sol-gel method (Liu *et al.*, 2000) and silver nanorods by an electrochemical technique (Zhu *et al.*, 2001) Bhattacharjee *et al.* (2002) proposed a method to synthesize CdS nanoparticles implanted in a matrix made up of PEG 300. Variation of PEG-300 concentration played a critical role in the size and orientation of formed PbS nanoparticles. Increase in [PEG] decreased the reaction rate. It leads to a decrease in film thickness and hence an increase in transmittance of film. At the same time, optical band gaps increase with an increase in [PEG] (Kaci *et al.*, 2010). 1D nanostructural materials are prepared by using structure-directing agents like PEG polymers (Shi *et al.*, 2007). Hexagonal ZnO micro nuts (HZMNs) were prepared in a hydrothermal method by using Zn(II)-PEG 300 globules as a soft template (Shi *et al.*, 2009). PEG-300 was used as a surfactant in a hydrothermal route for the preparation of rectangle rod-like shaped 4ZnO.B₂O₃.H₂O, which can be used as a flame-retardant filling material (Shi *et al.*, 2007). Similarly, the two-phase system consisting of PEG along with aqueous KCl, was used to extract the metal ions (like Zn⁺² and Cu⁺²) (Ammar *et al.*, 2011).

Ulbricht *et al.* (2014) reported the oxidative degradation of PEGs in appropriate conditions. (Per) Oxidation of PEGs is very well known (Han *et al.*, 1997). PEG 200 and 300 are degraded by *Alcaligenes faecalis* var. *denitrificans* during their anaerobic growth (Grant and Payne, 1983). Literature survey shows the oxidation of PEGs by different oxidants like ceric (IV) ions Szymanski *et al.* (2015) (Nagaranjan *et al.*, 1994), Mn/Ce composite oxide (Imamura *et al.*, 1986), permanganate (Hassan *et al.*, 2018), Jone's reagent (Lele and Kulkarni, 1998) and Fenton reagent (Chen *et al.*, 2014; Prousek and Duriskova, 1998). Since the oxidation of PEG-300 by periodate was not studied so far, it is considered for the current study.

MATERIALS AND METHODS

Different concentrations of oxidant (potassium periodate), the substrate (POE) were thermostatted at a constant temperature (35±0.1 °C) for two hours. In all the cases, substrate concentration was kept

higher compared to oxidant. Determined the unreacted oxidant concentration by iodometry. Reproducibility of reaction rate constants was found to be within ± 5%. Transfer of two electrons or loss of one atom of oxygen per oxidant molecule was measured, i.e., conversion of periodate up to iodate, as the latter is incapable of oxidizing the PEG-300 (POE) molecules. Iodate was used to conduct separate experiments to endorse the above reactions. Alkalinity was maintained by using sodium hydroxide. Taking into consideration of the maintained fair alkali concentrations in the present condition, its effect was studied. Reaction vessels surface has no effect on the reaction rate, and it was confirmed from the obtained identical results with acrylic and quartz ware. Dissolved oxygen has no influence on reaction as the difference is insignificant in the rate constants obtained in the presence of air and under nitrogen atmosphere.

RESULTS AND DISCUSSION

Reaction orders

Adopted the uni-variant method to determine the reaction orders w.r.t. concentrations of periodate / POE / alkali, in which rate constants were measured by changing the concentration of one variant while maintaining constant experimental conditions as well as concentrations of balance reagents involved (Table 1). Varied the periodate concentration over the range of 0.00025 to 0.002 M at fixed conditions of [POE], [OH⁻] and temperature (Table 1). Insignificant effect of periodate concentration on the reaction rate was noticed, i.e., pseudo-first-order rate constants (k₁) were almost constant with the variation of periodate concentration in the above range. First-order nature of reaction was also evident from the linearity of plots obtained in log [periodate] versus time (Figure 1).

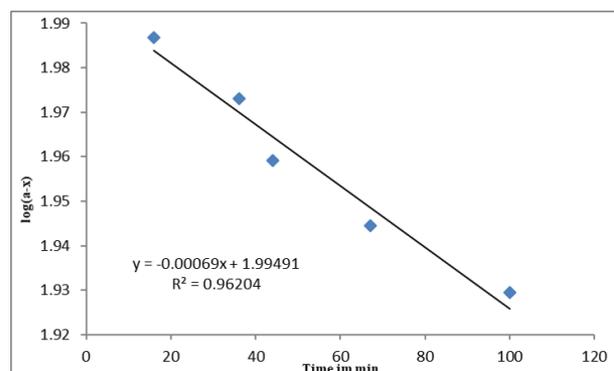


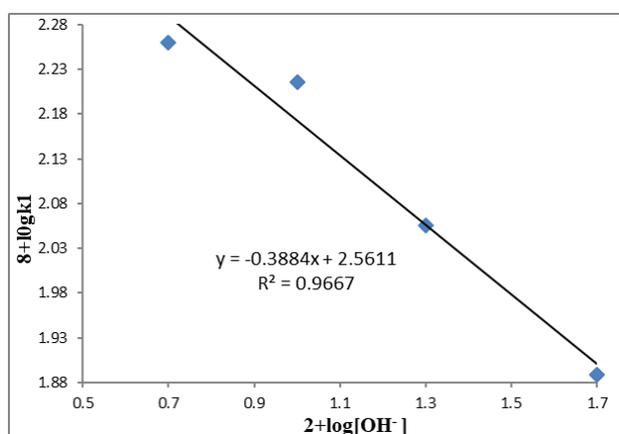
Figure 1: Plot of log(a-x) versus time at 35 °C and periodate (0.002 M), POE (0.025 M) and hydroxide (0.1 M)

Logarithmic values of rate constants were plotted

Table 1: Rate constants in the variation of reaction parameter values

[KIO ₄] M	[POE] M	[Alkali] M	Temp (°C)	k ₁ x 10 ⁴ min ⁻¹
0.00025	0.025	0.1	35	16.78
0.0005	0.025	0.1	35	16.42
0.0010	0.025	0.1	35	15.50
0.0020	0.025	0.1	35	14.67
0.0005	0.0025	0.1	35	16.94
0.0005	0.0125	0.1	35	17.15
0.0005	0.025	0.1	35	16.42
0.0005	0.050	0.1	35	17.99
0.0005	0.100	0.1	35	16.77
0.0005	0.025	0.05	35	18.20
0.0005	0.025	0.1	35	16.42
0.0005	0.025	0.2	35	11.36
0.0005	0.025	0.5	35	7.74
0.0005	0.025	0.1	35	16.42
0.0005	0.025	0.1	40	35.63
0.0005	0.025	0.1	45	55.27
0.0005	0.025	0.1	50	63.90

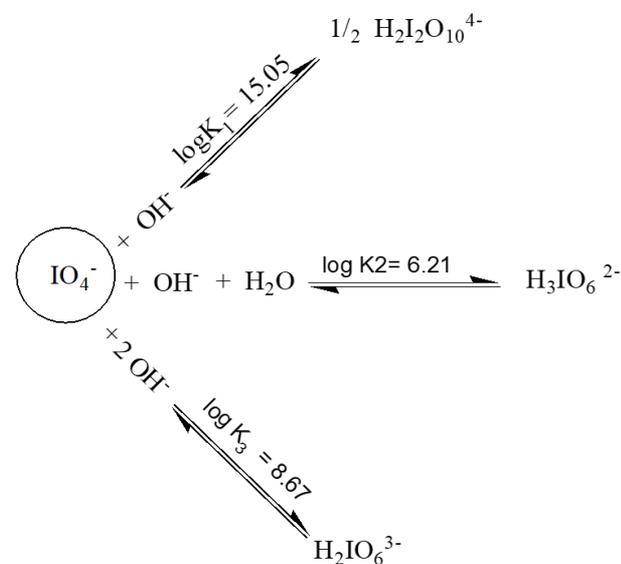
against logarithmic values of variant concentration, and the slope was used to determine the respective reaction order in the case of POE and hydroxide ion concentrations. Changed the substrate (POE / PEG-300) concentration from 0.0025 to 0.1 M and measured the reaction rates. It was found to be the reaction rate is independent of substrate concentration. Hence, the order was zero in the case of [POE] whereas, substrate inhibition was reported in the literature in the oxidation of different sugar alcohols under similar reaction conditions (Kumar *et al.*, 2014).

**Figure 2: Alkali effect on the rate of oxidation of POE**

Alkali concentration effect on the reaction rate was studied by increasing its concentration from 0.05 to 0.5 M. Retardation of rate was observed, which indi-

cates the inverse nature of the reaction. As the slope value was less than one (-0.388) in the plot of $\log k_1$ vs $\log [\text{OH}^-]$ (Figure 2), inverse fractional order in alkali concentration was concluded.

Equilibrium exists between potassium periodate and its dissociation products in alkaline medium (Aveston, 1969). Equations (1-3) along with concerned equilibrium constants (at 298.2 K) are given below.



Under these equilibrium conditions, the extent of periodate species availability in aq. alkaline condi-

tions can be calculated. At the maintained $[OH^-]$ $[IO_4^-]$, and $[H_2I_2O_{10}^{4-}]$ are insignificant among the possible four periodate species, whereas, higher concentrations are observed for $[H_3IO_6^{2-}]$ and $[H_2IO_6^{3-}]$ (i.e., species – 3 and 4). In a similar line to other researchers (Tuwar *et al.*, 1992; Shan *et al.*, 2005; Kulkarni and Nandibewoor, 2006), the concentrations of these two predominant species can be calculated by taking the help of Crouthamel *et al.* (1951). $[IO_4^-]_{ex}$ denotes the total concentration of periodate and is considered as equivalent to the sum of $[H_3IO_6^{2-}]$ and $[H_2IO_6^{3-}]$. Based on the two equilibrium conditions (2) and (3), (Shan *et al.*, 2009) has proposed two Equations (4) and (5).

$$\begin{aligned} & [H_2IO_6^{3-}] \\ &= \frac{\beta_3[OH^-]^2}{1 + \beta_2[OH^-] + \beta_3[OH^-]^2} [IO_4^-]_{ex} \quad (4) \\ &= f([OH^-])[IO_4^-]_{ex} \end{aligned}$$

$$\begin{aligned} & [H_3IO_6^{2-}] \\ &= \frac{\beta_2[OH^-]}{1 + \beta_2[OH^-] + \beta_3[OH^-]^2} [IO_4^-]_{ex} \quad (5) \\ &= \phi([OH^-])[IO_4^-]_{ex} \end{aligned}$$

In molar units, hydroxide concentrations (corresponding $[H_3IO_6^{2-}]$ & $[H_2IO_6^{3-}]$) are 0.025 (0.000107 & 0.000364), 0.05 (0.000180 & 0.000308), 0.10 (0.000267 & 0.000228), 0.20 (0.000349 & 0.000149) and 0.50 (0.000427 & 0.000073). It shows a simultaneous increase in $[H_2IO_6^{3-}]$ and decrease in $[H_3IO_6^{2-}]$ with an increase in $[OH^-]$. These two predominant periodate species complex with POE-300.

Activation parameters

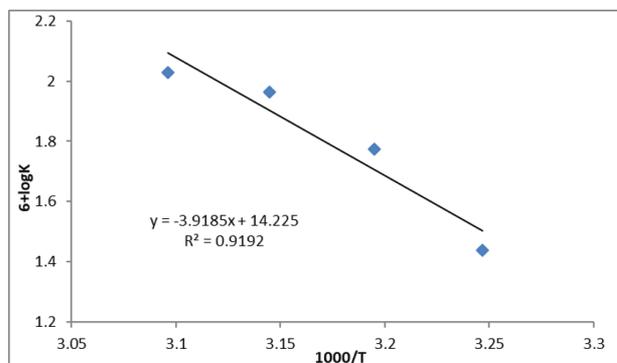


Figure 3: Effect of temperature on rate reaction

Studied the effect of temperature on the reaction rate by measuring first-order constants (k_1) at 35, 40, 45 and 50 °C. Values of k_1 increased with an increase of temperature. Least squares method was

applied to the plot of $\log k_1$ versus $1/T$ (Figure 3). Eyring equation (Wynne-Jones and Eyring, 1935) was used to determine activation parameters

$$(\Delta E^\ddagger, \Delta H^\ddagger, \Delta G^\ddagger \text{ and } -\Delta S^\ddagger)$$

and the values are presented in Table 2.

Effect of added boric acid and salts

Kumar *et al.* (2012, 2014) studied the effect of boric acid presence on sugar alcohols oxidation by periodate in alkaline medium. The increased reaction rate was attributed to a favourable environment for the formation of a complex between borate ion and sugar alcohols, which contributes to the substrate inhibition. But no appreciable effect of boric acid is noticed in the present case (Table 3). It can be explained taking into consideration of the presence of more hydroxyl groups on POE (PEG-300) as its hydroxyl value ranges between 340 and 394 (html link). Though, some of the hydroxyl groups of POE complex with borate ions, a good number of free -OH will be available on the substrate. Inclusion of bromide ions increased the reaction rate, but in the contrary, a retarded reaction rate was observed with the other two halide ions (chloride, iodide).

Effect of solvent:

To study the effect of solvent on the reaction rate, the reaction was carried out at different proportions of t-butyl alcohol and water (Table 4). The addition of t-butyl alcohol reduced the rate of reaction, indicating that a decrease in the dielectric constant of the medium reduces the reaction rate.

Rate law equation

Long-chain Carboxylic acids were the minor products along with aldehydes as the prime reaction products in the oxidation of POE by periodate in alkaline medium. Spot tests were used to detect so formed products (Feigl, 1956). Aldehydes formation in the present study was further confirmed by converting to 2,4-dinitrophenylhydrazones. Szymanski *et al.* (2015) reported the products with the same nature. It shows that terminal -OH groups are active, which corroborates with the common name of these substrates as 'polyethylene glycols' (Henning, 2001). Moreover, its hydroxyl value is practically high. So, the observed final products can be understood from terminal -OH groups oxidation. However, stoichiometry was unable to determine accurately. Derived a suitable rate law as given below, by considering the reactions orders in oxidant, substrate and alkali.

Table 2: Arrhenius parameters at 308 k

ΔE^\ddagger KJ/mole	ΔH^\ddagger KJ/mole	ΔS^\ddagger JK ⁻¹ / mole	$\log_{10} P_z$	ΔG^\ddagger KJ/mole
75.02	72.46	97.34	8.16	102.44

Table 3: Reaction rate variation with salt concentration

Salt	[Salt] M	$k_1 \times 10^4 \text{ min}^{-1}$
Nil	Nil	16.42
KCl	0.1	12.80
KBr	0.1	25.71
KI	0.1	4.29
KNO ₃	0.1	15.90
Boric Acid	0.01	15.43
Boric Acid	0.025	14.91
Boric Acid	0.05	15.80

[periodate] = 0.0005 M [POE] = 0.025 M
Temperature = 35°C [OH⁻] = 0.1 M

Table 4: Effect of solvent

t-butyl alcohol : water (v/v)	$k_1 \times 10^4 \text{ min}^{-1}$
0 : 100	16.42
5 : 95	6.98
10 : 90	6.56
20 : 80	6.68
40 : 60	6.63

C₁ and C₂ are the complexes formed between the substrate (POE) and the active species -of periodate ([H₃IO₆²⁻] and [H₂IO₆³⁻]). Then the products are formed by rate-determining dissociation of these complexes.



$$\text{Rate} = k_1 [C_1] + k_2 [C_2] = [IO_4^-] [OH^-] [S] \{k_1 K_2 K_4 + k_2 K_3 K_5 [OH^-]\}$$

Out of [IO₄⁻], H₂I₂O₁₀⁴⁻, H₃IO₆²⁻, H₂IO₆³⁻, Complex C₁ and Complex C₂, the first two species are negligible, overall periodate concentration, [IO₄⁻]_T is rewritten as given below.

$$[IO_4^-]_T = [\text{species-3}] + [\text{species-4}] + [C_1] + [C_2]$$

As the hydroxyl values of POE (PEG-300) is in the range of 340-394 (html link), a large number of -OH are available and hence, species-3 and species-4 are completely complexed with them. Therefore, concentrations of those two species can be neglected to rewrite the above equation as

$$[IO_4^-]_T = [C_1] + [C_2] = K_2 K_4 [S] [IO_4^-] [OH^-] + K_3 K_5$$

$$[S] [IO_4^-] [OH^-]^2$$

The above equation can be rearranged to get

$$[IO_4^-] = \frac{[IO_4^-]_T}{[OH^-][S] \{K_2 K_4 + K_3 K_5 [OH^-]\}}$$

By substituting the value of [IO₄⁻] in the rate expression, we can conclude that

$$\text{Rate} = \frac{[IO_4^-]_T \{k_1 K_2 K_4 + k_2 K_3 K_5 [OH^-]\}}{\{K_2 K_4 + K_3 K_5 [OH^-]\}}$$

The above rate law explains the observed reaction orders (first order in [oxidant] and independence of reaction to [substrate]). In comparison to the denominator, the value of [OH⁻] value in the numerator is small due to k₂ << 1. And hence, inverse fractional order in [OH⁻] can be explained.

CONCLUSIONS

Periodate oxidation of POE (or PEG-300, a key polymer in the pharmaceutical industry) followed first order kinetics in [oxidant], independent of [substrate] and inverse fractional order in [OH⁻]. Postulated a suitable rate by considering the experimental results.

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REFERENCES

- Ammar, S. H., Abdul-Nabi, W. A. W., Rasheed, M. K. 2011. Extraction of Zn (II) and Cu (II) Ions Using PEG (300) - KCl Salt Aqueous Two-Phase Systems. *Al-Khwarizmi Engineering Journal*, 7(2):68–74.
- Antwerp, W. V., Gulati, P. S., Adomian, G. E. 2002. Medtronic Minimed Inc, assignee. Medication device with protein stabilizing surface coating. U.S. Patent No. 6,443,942.
- Aveston, J. 1969. Hydrolysis of potassium periodate: ultracentrifugation, potentiometric titration, and Raman spectra. *Journal of the Chemical Society A: Inorganic, Physical, Theoretical*, pages 273–275.
- Bailey, Koleske 1976. *Poly(Ethylene Oxide)*, Academic Press, New York.
- Bendale, P. M., Khadilkar, B. M. 2000. Selective Hydrolysis of Nitriles to Amides Using NaOH-PEG Under Microwave Irradiation. *Synthetic Communications*, 30(10):1713–1718.
- Bhattacharjee, B., Ganguli, D., Chaudhuri, S. 2002. Luminescent CdS nanoparticles embedded in polyethylene glycol (PEG 300) matrix thin film. *Journal of Nanoparticle Research*, 4(3):225–230.
- Cartotto, Peters, Neligan, Douglas, Beeston 1996. Chemical burns. *Canadian journal of surgery*, 39(3):205.
- Chen, X., Gao, L. J., Gu, F. 2014. Fenton Oxidation of Different Molecular Weights Polyethylene Glycols in Wastewater. *Advanced Materials Research*, 1033:382–386.
- Crouthamel, C. E., Hayes, A. M., Martin, D. S., *et al.* 1951. Ionization and Hydration Equilibria of Periodic Acid. *Journal of the American Chemical Society*, 73(1):82–87.
- Debotton, N., Dahan, A. 2017. Applications of Polymers as Pharmaceutical Excipients in Solid Oral Dosage Forms. *Medicinal Research Reviews*, 37(1):52–97.
- D'souza, A. A., Shegokar, R. 2016. Polyethylene glycol (PEG): a versatile polymer for pharmaceutical applications. *Expert Opinion on Drug Delivery*, 13(9):1257–1275.
- Dziurka, D. 2005. Properties of particleboards resinated with PMDI resin modified with ethylene glycol and PEG 300. *Folia Forestalia Polonica. Series B-Drzewnictwo*, 36.
- Feigl 1956. *Spot Tests in Organic Analysis*, Elsevier Publishing Co. page 208.
- Grant, M. A., Payne, W. J. 1983. Anaerobic growth of *Alcaligenes faecalis* var. *denitrificans* at the expense of ether glycols and nonionic detergents. *Biotechnology and Bioengineering*, 25(2):627–630.
- Han, S., Kim, C., Kwon, D. 1997. Thermal/oxidative degradation and stabilization of polyethylene glycol. *Polymer*, 38(2):317–323.
- Hassan, R., Ibrahim, S., Sayed, S. 2018. Kinetics and mechanistic aspects on electron-transfer process for permanganate oxidation of poly(ethylene glycol) in aqueous acidic solutions in the presence and absence of Ru(III) catalyst. *International Journal of Chemical Kinetics*, 50(11):775–783.
- Henning, T. 2001. Polyethylene glycols (PEGs) and the pharmaceutical industry. *Fine, Specialty & Performance*, 127:28–32.
- Imamura, S., Nakamura, M., Kawabata, N., Yoshida, J., Ishida, S. 1986. Wet oxidation of poly(ethylene glycol) catalyzed by manganese-cerium composite oxide. *Industrial & Engineering Chemistry Product Research and Development*, 25(1):34–37.
- Kaci, S., Keffous, A., Trari, M., Menari, H., Manseri, A., Mahmoudi, B., Guerbous, L. 2010. Influence of polyethylene glycol-300 addition on nanostructured lead sulfide thin films properties. *Optics Communications*, 283(17):3355–3360.
- Kulkarni, S. D., Nandibewoor, S. T. 2006. A kinetic and mechanistic study on oxidation of Isoniazid drug by alkaline diperiodatocuprate(III) – A free radical intervention. *Transition Metal Chemistry*, 31(8):1034–1039.
- Kumar, Y. L., Nadh, R. R. V., Radhakrishnamurti, P. S. 2012. Kinetics of oxidation of myo-inositol by potassium periodate in alkaline medium. *Asian Journal of Chemistry*, 24(12):5869–5872.
- Kumar, Y. L., Nadh, R. V., Radhakrishnamurti, P. S., *et al.* 2014. Substrate inhibition: Oxidation of D-sorbitol and D-mannitol by potassium periodate in alkaline medium. *Russian Journal of Physical Chemistry A*, 88(5):774–778.
- Lele, B. S., Kulkarni, M. G. 1998. Single step room temperature oxidation of poly(ethylene glycol) to poly(oxyethylene)-dicarboxylic acid. *Journal of Applied Polymer Science*, 70(5):883–890.
- Liu, X., Yang, J., Wang, L., Yang, X., Lu, L., Wang, X. 2000. An improvement on sol-gel method for preparing ultrafine and crystallized titania powder. *Materials Science and Engineering: A*, 289(1–

- 2):241–245.
- Nagarajan, S., Srinivasan, K. S. V., Rao, K. V. 1994. Kinetic and Mechanistic Studies on the Oxidation of Poly(ethylene glycol) by Ceric Sulphate in Sulphuric Acid Medium. *Polymer Journal*, 26(7):851–857.
- Prousek, Duriskova 1998. Oxidative degradation of poly (ethylene glycol) s (PEG) by the Fenton and photo-Fenton reactions. *Chemické listy*, 92:218–220.
- Razler, T. M., Hsiao, Y., Qian, F., Fu, R., Khan, R. K., Doubleday, W. 2009. A Preparatively Convenient Ligand-Free Catalytic PEG 2000 Suzuki–Miyaura Coupling. *The Journal of Organic Chemistry*, 74(3):1381–1384.
- Sauvagnat, B., Lamaty, F., Lazaro, R., Martinez, J. 2000. Poly(ethylene glycol) as solvent and polymer support in the microwave assisted parallel synthesis of aminoacid derivatives. *Tetrahedron Letters*, 41(33):6371–6375.
- Savino, F., Viola, S., Erasmo, M., Nardo, G. D., Oliva, S., Cucchiara, S. 2012. Efficacy and tolerability of peg-only laxative on faecal impaction and chronic constipation in children. A controlled double blind randomized study vs a standard peg-electrolyte laxative. *BMC Pediatrics*, 12(1):178.
- Shan, J., Wang, H., Song, C., Wang, F. 2009. Kinetics and mechanism of oxidation of 2-amino-1-butanol by diperiodatoargentate(III) in alkaline medium. *Bulletin of the Chemical Society of Ethiopia*, 23(2):297–302.
- Shan, J. H., Li, S. M., Huo, S. Y., Shen, S. G., Sun, H. W. 2005. Kinetics and mechanism of the oxidation of β -alanine by dihydroxydiperiodatoargentate(III) in an alkaline medium. *Journal of the Iranian Chemical Society*, 2(3):226–231.
- Sharghi, H., Khalifeh, R., Rashidi, Z. 2013. Synthesis of chromeno[3,4-b]quinoline derivatives by heterogeneous [Cu(II)BHPPDAH] catalyst without being immobilized on any support under mild conditions using PEG 300 as green solvent. *Molecular Diversity*, 17(4):721–730.
- Shi, X., Li, M., Yang, H., Chen, S., Yuan, L., Zhang, K., Sun, J. 2007. PEG-300 assisted hydrothermal synthesis of 4ZnO·B₂O₃·H₂O nanorods. *Materials Research Bulletin*, 42(9):1649–1656.
- Shi, X., Pan, L., Chen, S., Xiao, Y., Liu, Q., Yuan, L., Cai, L. 2009. Zn(II)-PEG 300 Globules as Soft Template for the Synthesis of Hexagonal ZnO Micronuts by the Hydrothermal Reaction Method. *Langmuir*, 25(10):5940–5948.
- Silva, A. 2010. Ligand-free Suzuki–Miyaura reactions in PEG 300. *Tetrahedron Letters*, 51(30):3883–3885.
- Szymanski, J. K., Temprano-Coletto, F., Pérez-Mercader, J., *et al.* 2015. Unusual kinetics of poly(ethylene glycol) oxidation with Cerium(IV) ions in sulfuric acid medium and implications for copolymer synthesis. *Physical Chemistry Chemical Physics*, 17(10):6713–6717.
- Tuwar, S. M., Nandibewoor, S. T., Raju, J. 1992. Oxidation of allyl alcohol by diperiodatonickelate (IV) in aqueous alkaline medium. *Journal of Indian Chemical Society*, 69:651.
- Ulbricht, J., Jordan, R., Luxenhofer, R. 2014. On the biodegradability of polyethylene glycol, polypeptides and poly(2-oxazoline)s. *Biomaterials*, 35(17):4848–4861.
- Wynne-Jones, W. F. K., Eyring, H. 1935. The Absolute Rate of Reactions in Condensed Phases. *The Journal of Chemical Physics*, 3(8):492–502.
- Xie, X. J., Yang, G. S., Cheng, L., Wang, F. 2000. Huaxue Shiji. Chinese.] [ChemPort, 22:222–223.
- Xu, M., Zhang, C. Y., Wu, J., Zhou, H., Bai, R., Shen, Z., Liu, J. 2019. PEG-Detachable Polymeric Micelles Self-Assembled from Amphiphilic Copolymers for Tumor-Acidity-Triggered Drug Delivery and Controlled Release. *ACS Applied Materials & Interfaces*, 11(6):5701–5713.
- Yin, L., Zhang, Z., Wang, Y. 2006. PEG (300)–PdCl₂ promoted efficient and convenient Suzuki–Miyaura coupling of aryl chlorides with arylboronic acids. *Tetrahedron*, 62(40):9359–9364.
- Zhang, Z. H., Yin, L., Wang, Y. M., Liu, J. Y., Li, Y. 2004. Indium tribromide in poly(ethylene glycol)(PEG): a novel and efficient recycle system for chemoselective deprotection of 1,1-diacetates. *Green Chemistry*, 6(11):563.
- Zhu, J. J., Liao, X. H., Zhao, X. N., Chen, H. Y. 2001. Preparation of silver nanorods by electrochemical methods. *Materials Letters*, 49(2):91–95.