Biomimetic polymerization of acrylamide with hydrogen peroxide catalyzed by water-soluble anionic iron(III) 5,10,15,20-tetrakis-(2′,6′-dichloro-3′-sulfonatophenyl)porphyrin

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Dedicated to Professor P.T. Narsimahan on his 75th birth anniversary

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Abstract

The biomimetic polymerization of acrylamide (**1**) with hydrogen peroxide catalyzed by water soluble iron(III) 5,10,15,20-tetrakis-(2′,6′-dichloro-3′-sulfonatophenyl)porphyrin (**3**) gave high yield of polyacrylamide (**2**) in the molecular weight range of 1,30,000-1,50,000 g mol^{-1} in the absence and presence of 2,4-pentanedione at an ambient temperature in nitrogen atmosphere. The molar ratio of **3**: H_2O_2: **1** was 1: 100: 3300. Yields were high at pH 4.5 but dropped at pH 7.2. Finally no polymer was formed at pH 9.2 in the absence of 2,4-pentanedione, whereas the yield raised to 99% in the presence of 2,4-pentanedione.

Keywords: Iron(III) 5,10,15,20-tetrakis-(2′,6′-dichloro-3′-sulfonatophenyl)porphyrin, hydrogen peroxide, biomimetic polymerization, polyacrylamide

Introduction

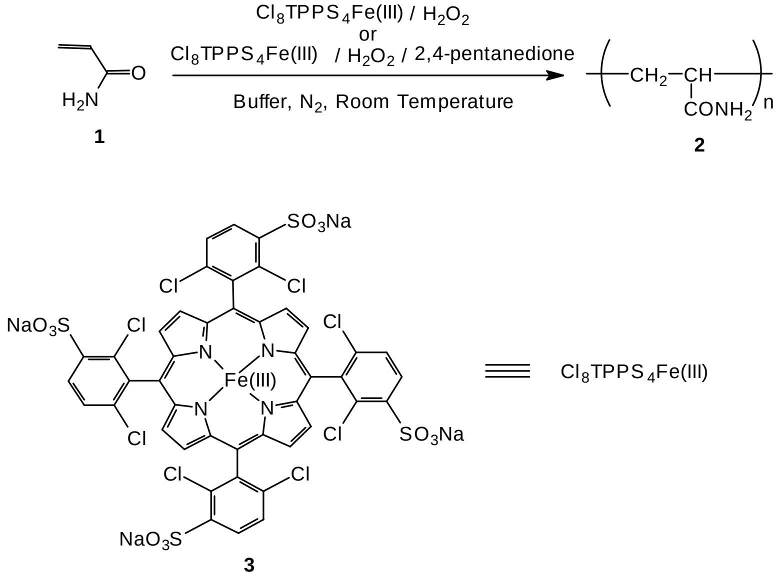
Enzymatic catalysis is involved in both in-vivo and in-vitro polymerizations.[1-3] Various biopolymers and non-natural synthetic polymers have been synthesized under ecofriendly and milder conditions by enzyme-catalyzed polymerizations. A selective enzyme catalyzes a specific polymerization reaction with high selectivity. Glycosidase specifically catalyses the synthesis of various natural and unnatural polysaccharides under much milder conditions with high yields.[4,5] Lipase catalyses the synthesis of optically active polyesters and transesterification of polyesters to produce random copolyesters,[6,7] whereas papain catalyses the polymerization of amino acids.[8] Oxidoreductases including peroxidase, laccase and bilirubin oxidase are used as catalysts by the production of novel polyphenolics and related compounds.[9]

The reaction of phenols and anilines with hydrogen peroxide catalyzed by different oxidoreductases is an alternative ecofriendly route to synthesize the industrially important polyaromatics.[9-16] Similarly the vinylic monomers have also been polymerized with hydrogen peroxide catalyzed by HRP and related enzymes under milder conditions with high yields.[11,17-20]

Lipid-soluble and water-soluble metalloporphyrins mimic the various reactions of cytochrome P450, HRP and other monooxygenases in different reactions.[21,22] Herein, we report a novel route for the polymerization of acrylamide with hydrogen peroxide catalyzed by anionic water-soluble iron(III) 5,10,15,20-tetrakis-(2′,6′-dichloro-3′-sulfonatophenyl)porphyrin to understand the molecular mechanism of peroxidase and related oxidoreductase enzymes and their utilization in polymerization reactions.

Results and Discussion

Screening of $Cl_8TPPS_4Fe(III)$ (3) as catalyst in polymerization of acrylamide (1). The reaction of **1** (7mmol) with H_2O_2 (0.106 mmol) in the absence of **3** gave no polymer (**Table1, entry1**). The reaction of **1** (7mmol) with H_2O_2 (0.106 mmol) catalyzed by **3** (2.12×10^{-3} mmol) gave polymer **2** (**Scheme 1**) in 85% yield (**Table 1, entry 3**).



Scheme 1. Polymerization of acrylamide (**1**) with hydrogen peroxide catalyzed by $Cl_8TPPS_4Fe(III)$ (**3**).

The formation of polymer **2** was indicated in the absence of a peak at 1612 cm^{-1} for olefinic stretching and a carbonyl absorption from 1672 to 1655 cm^{-1} in its IR spectra. The disappearance of signals for olefinic protons at δ 5.10 and the appearance of characteristic broad signals at δ 1.59 and 2.16 corresponding to the methylene and methine protons in the ^{1}H-NMR spectra confirmed the formation of **2**. The average molecular weight of **2** was found to be 1,30,000 g mol^{-1} by the viscosity measurements in water at 25°C.[23] The complete thermal degradation of **2** occurred in two stages at 315°C and 423°C when the rate of heating was 5°C/min in their thermogravimetric analysis[24] (**Figure 1**). The ratio of **3**: H_2O_2: **1** as 1: 100: 3300 was found to be suitable for the polymerization of **1** at room temperature.

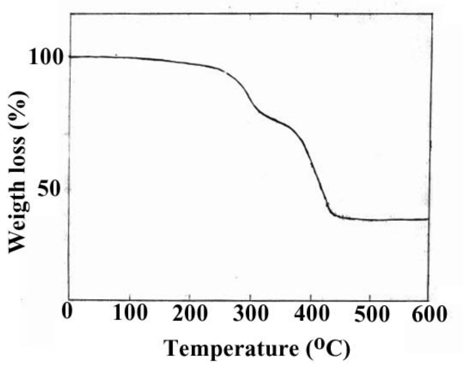


Figure 1. Thermogravimetric analysis of **2** with temperature.

Polymerization of 1 with H_2O_2 catalyzed by $Cl_8TPPS_4Fe(III)$ (3) in different reaction conditions. The reaction of **1** with H_2O_2 catalyzed by robust $Cl_8TPPS_4Fe(III)$ (**3**) was carried out in acetate buffer (pH 4.5, 0.2M) at an ambient temperature in a nitrogen atmosphere. The monomer **1** was quantitatively consumed to give the polymer **2** in 85% yield (**Table 1**, **entry 3**). The yield of **2** dropped to 5% at pH 7.2 while there was no detectable amount of polymer at pH 9.2 under the same conditions (**Table 1**, **entry 7** and **11**).

Table 1. Effect of pH and the presence of 2,4-PD on the polymerization of **1** with H_2O_2 catalyzed by **3**

S. No.	System [a]	Yield [b] %	Mol. Wt, M_n (g mol^{-1}) [c]	Polydispersity
1.	H_2O_2 / pH 4.5	-	-	-
2.	H_2O_2 / 2,4-PD[d] / pH 4.5	-	-	-
3.	**3** / H_2O_2 / pH 4.5	85	1,30,000	2.45
4.	**3** / H_2O_2 / 2,4-PD / pH 4.5	98	1,50,000	2.40
5.	H_2O_2 / pH 7.2	-	-	-
6.	H_2O_2 / 2,4-PD / pH 7.2	-	-	-
7.	**3** / H_2O_2 / pH 7.2	5	N.D.	-
8.	**3** / H_2O_2 / 2,4-PD / pH 7.2	15	N.D.	-
9.	H_2O_2 / pH 9.2	-	-	-
10.	H_2O_2 / 2,4-PD / pH 9.2	-	-	-
11.	**3** / H_2O_2/ pH 9.2	-	-	-
12.	**3** / H_2O_2 / 2,4-PD / pH 9.2	99	51,000	2.90

[a] Ratio of system **3** : H_2O_2 : **1** = 1: 100 : 3300.

3: H_2O_2 : 2,4-PD : **1** = 1: 100 : 110 : 3300.

[b] Yield corresponds to weight of **2** obtained to the weight of **1** used.

[c] Determined by viscosity measurements at 25°C using $[\eta] = 6.8 \times 10^{-4} M_n^{0.66}$ and $[\eta] = 6.31 \times 10^{-4} M_w.^{0.80}$

[d] 2,4-PD = 2,4-Pentanedione, N.D.= Not determined (due to low yield).

Effect of 2,4-pentanedione (2,4-PD) on polymerization of 1 at different pH′s. The addition of 2,4-PD to the reaction of **1** with H_2O_2 catalyzed by **3** at pH 4.5 and 7.2 enhanced the yield of polymer **2** to 98 and 15% respectively (**Table 1, entry 4** & **8**). The polyacrylamide (**2**) obtained at pH 4.5 in the presence of 2,4-PD was of comparable molecular weight and polydispersity to that obtained in the absence of 2,4-PD (**Table 1, entry 3** & **4**). At pH 9.2, the addition of 2,4-PD to the above reaction facilitated the polymerization of **1** and produced the polymer **2** of low molecular weight (51,000 g mol$^-$1) and polydispersity 2.90 in 99% yield (**Table 1, entry 12**).

The polymer was obtained in 40% and 70% yield when the ratio of **3** and 2,4-PD was 1 : 5 and 1: 50 respectively at pH 9.2. The optimal ratio of **3** and 2,4-PD was found to be 1 : 110 under given reaction conditions to obtain the polymer in 99% yield. Further increase in the concentration of 2,4-PD gave decreased product yield.

The effect of pH on the % yield of the polymer in the absence and the presence of 2,4-PD is also summarized in the **Figure 2**.

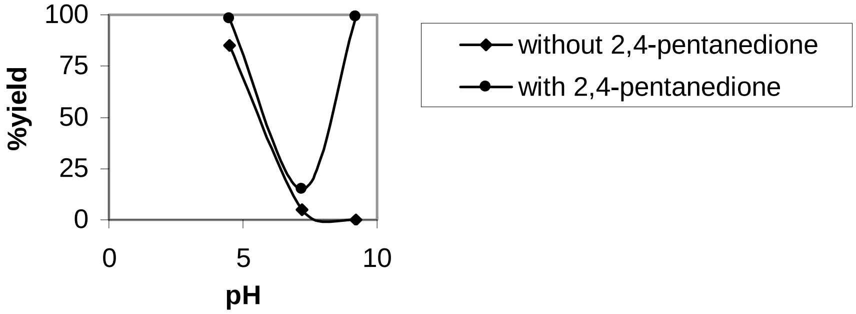


Figure 2. Effect of pH on the %yield of the polymer (**2**) in the absence and the presence of 2,4-PD.

Effect of reaction time on the molecular weight of 2. The effect of the reaction time on the molecular weight of **2** is shown in **Figure 3**. As the reaction time increases the molecular weight of polyacrylamide increases, which indicates the free radical behaviour of the process.

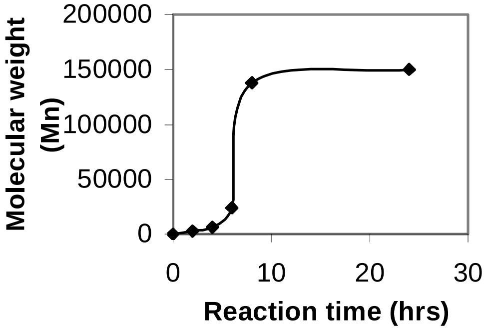
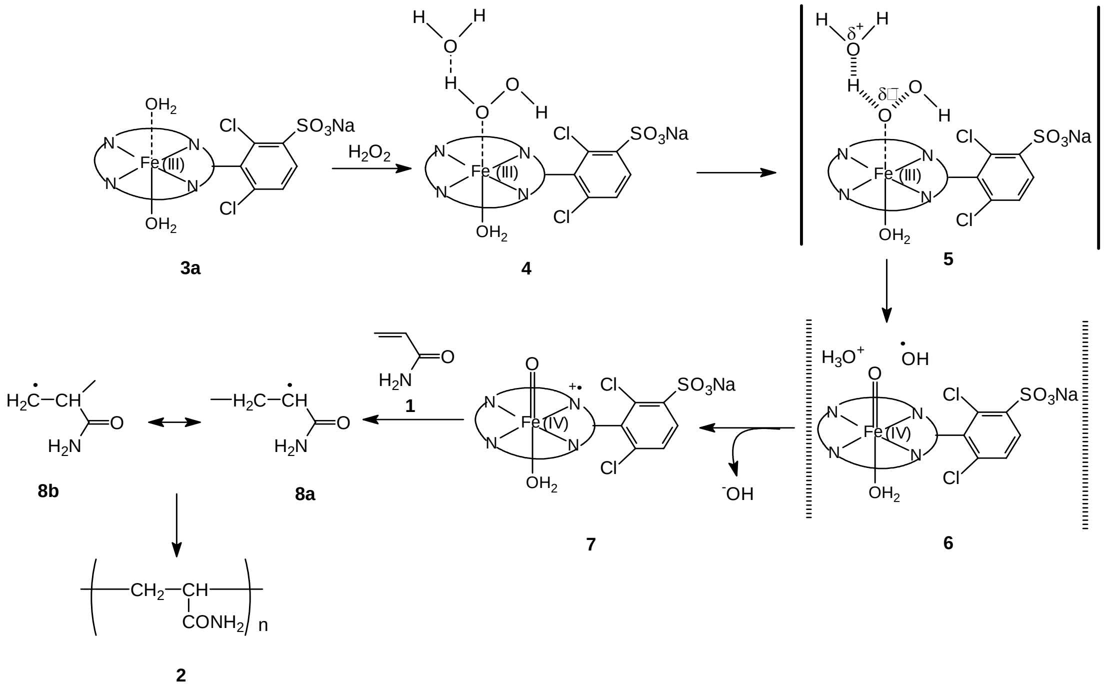


Figure 3. Changes in molecular weight of **2** produced at pH 4.5 (10 mL of 0.2M acetate buffer) using **3** : H_2O_2 : 2,4-PD : **1** in the ratio 1 : 100 : 110 : 3300 at room temperature at different reaction times.

Comparison of polymerization reaction of HRP with water-soluble $Cl_8TPPS_4Fe(III)$ (3). The reaction of 1 with H_2O_2 catalyzed by HRP at pH 4.5 in a nitrogen atmosphere gave the polymer in 60% yield at room temperature, the concentrations being [HRP]= $2gL^{-1}$, [**1**]= 0.46M and [H_2O_2]= 11mM. No polymer was obtained at pH 9.2 under the same conditions due to deactivation of HRP enzyme at higher pH. This kind of HRP-catalyzed polymerization of vinylic monomers has been reported using large quantities of H_2O_2 (either 1/1 or 9/1 molar ratio) with respect to monomer.[11,19] The formation of oxoiron(IV) radical cation by the reaction of HRP and H_2O_2 has been proposed to be responsible for the polymerization reaction.

Water-soluble $Cl_8TPPS_4Fe(III)$ (**3**) has been used as a model for HRP to mimic their various reactions. At acidic pH, iron(III) porphyrin exists as -Fe(III)$(H_2O)_2$- (**3a**).[25,26] On the addition of H_2O_2 to **3a**, the species -Fe(III)(OOH)(H-$_2$O)- (**4**) is generated. **4** then spontaneously gives the highvalent oxoiron(IV) radical cation (**7**) through the transient intermediates **5** and **6**. The intermediate **7** is responsible for initiating the formation of acrylamide radical (**8a** and **8b**), which attacks the other acrylamide molecule to form a bigger free radical and hence the reaction further propagates to give the polymer **2**. The reaction is terminated either by the combination of two bigger radicals or by abstraction of a proton from the solvent or another monomer molecule (**Scheme 2**). The stable dimethoxyiron(IV) porphyrin is generated by reaction of iron(III)porphyrin with H_2O_2 in presence of large excess of methanol.[27] Thus the polymerization of 1 is quenched by the addition of large excess of methanol. The formation of intermediate 7 could be explained only by the heterolytic cleavage of H_2O_2, which leads to the polymerization. This was confirmed as no polymer was obtained in the presence of H_2O_2 and absence of 3 (**Table 1, entry 1**).



Scheme 2. Proposed mechanism for the formation of reactive intermediate in polymerization of **1** with hydrogen peroxide catalyzed by $Cl_8TPPS_4Fe(III)$ (**3**).

At neutral and near alkaline pH, the peroxide anion ($^-$OOH) from H_2O_2 is not able to replace the axial ligand OH on -Fe(III)(H_2O)(OH)-, which is the species when **3** is present in the buffer of neutral and higher pH. Thus the concentration of highvalent oxoiron(IV) radical cation (**7**) decreases and hence very low or no polymerization is observed at these pH's.

The polymerization of vinylic monomers with H_2O_2 catalyzed by HRP in the presence of 2,4-PD and other β-diketones increases the yield of polymer significantly.[17-18,20] Polyacrylamide of molecular weight 1,24,000 g mol^{-1} and polydispersity 2.5 has been obtained by the polymerization of **1** with hydrogen peroxide catalyzed by HRP in the presence of 2,4-PD using H_2O_2-to-monomer ratio of 1/66 mol/mol at pH 5.1 while no polymer is reported in the absence of 2,4-PD.[17] Thus 2,4-PD was added to the reaction of **1** with H_2O_2 catalyzed by $Cl_8TPPS_4Fe(III)$ (**3**) at pH 4.5 and 7.2 and it enhanced the yield of polymer **2** to 98 and 15% respectively. At pH 4.5, the polymer **2** of comparable molecular weight (1,30,000 g mol^{-1}) and polydispersity (2.45) was obtained when **3** was used as the catalyst in place of HRP without any need for the addition of 2,4-PD. The addition of 2,4-PD at pH 9.2 offered a new route for polymerization of **1** at this pH, where the use of HRP is limited owing to its deactivation. The reaction of **1** with H_2O_2 in the presence of 2,4-PD in the absence of **3** produced no polymer (**Table 1**, **entry 10**). At pH 9.2, the reaction of **3** with H_2O_2 in the presence of 2,4-PD may produce a stable intermediate which contributes to the facile polymerization of **1** at this pH.

The large excess of H_2O_2 with respect to the monomer resulted in the degradation of the iron(III) porphyrin. Thus, a 1:66 molar ratio of H_2O_2 to monomer was found to be suitable for the polymerization of **1** both in the absence and the presence of 2,4-PD.

Conclusions

The water soluble anionic $Cl_8TPPS_4Fe(III)$ (**3**) in the presence of hydrogen peroxide is an economical and suitable system to initiate the polymerization of acrylamide at acidic and neutral pH, by using the molar ratio of **3**: H_2O_2 : **1** as 1 : 100 : 3300. The addition of 2,4-PD in this system enhances the yield of the polymer at both acidic and neutral pH and also facilitates the polymerization of **1** at alkaline pH, where HRP is deactivated. Thus the water-soluble anionic iron(III) porphyrin and H_2O_2 mimic the polymerization reaction of oxidoreductase enzyme HRP in the presence or absence of 2,4-PD under milder conditions with excellent yield.

Experimental Section

Material and methods. 1 and 2,4-PD were obtained from Biochemicals unit, India and Merck, Munchen, respectively and were also purified before use. The aqueous hydrogen peroxide (30% v/v) was obtained from CDH India and used without further purification. The 5,10,15,20-tetrakis-(2′,6′-dichloro-3′-sulfonatophenyl)porphyrin (H_2Cl_8TPPS-$_4$) was prepared by sulphonation of 5,10,15,20-tetrakis-(2′,6′-dichlorophenyl)porphyrin (Cl_8TPPH_2) with oleum at 130°C by following the literature procedure and metallated with ferrous chloride in DMF.[28,29]

The average molecular weight of polyacrylamide was determined from intrinsic viscosity measurements according to Mark-Houwink equations.[23] Viscosity measurements were obtained at 25°C in water using ubbelohde viscometer and $[\eta]_{c\rightarrow 0}$ was evaluated by the extrapolation of experimental data. $[\eta]_{c\rightarrow 0}$ values were used to calculate the number and weight average molecular weight according to the relations $[\eta] = 6.8 \times 10^{-4}\ M_n^{0.66}$ and $[\eta] = 6.31 \times 10^{-4}\ M_w^{0.80}$. ^{1}HNMR spectra were recorded on a Bruker Avance Spectrospin 300MHz spectrophotometer. Perkin Elmer FT-IR Spectrum 2000 Spectrometer was used to record IR spectra. Thermogravimetric analysis was obtained on a Rigaku Thermoflex, PTC-10A.

Polymerization of 1 with hydrogen peroxide catalyzed by water-soluble $Cl_8TPPS_4Fe(III)$ (3). The solution of **1** (7 mmol in 10mL acetate buffer of pH 4.5) was charged into a three-necked round-bottomed flask and degassed for 15 minutes. $Cl_8TPPS_4Fe(III)$ (2.12×10^{-3} mmol in 0.5 mL buffer) and 30% H_2O_2 (0.106 mmol) were successively injected into the above flask under stirring. The reaction was stirred for a predetermined time at an ambient temperature under a nitrogen atmosphere. The polymer was obtained by quenching the reaction with a large excess of methanol and filtered off, washing with methanol and drying under vacuum at 50°C. The yield and molecular weight of polymers are given in **Table1**.

Polymerization of 1 with hydrogen peroxide catalyzed by water-soluble $Cl_8TPPS_4Fe(III)$ (3) in the presence of 2,4-PD. The procedure and molar ratio of reactant (**1**) and catalyst (**3**) used in this case were exactly the same as mentioned above except for the addition of 2,4-PD (0.18 mmol) which was added simultaneously along with hydrogen peroxide. The results obtained in this case are also summarized in **Table 1**.

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