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ANALYTICAL SOLUTION OF THE CONCENTRATION OF SUBSTRATE AND EFFECTIVENESS FACTOR FOR ACETOPHENONE IN PACKED BED REACTOR

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ABSTRACT

A mathematical model of bioreduction of acetophenone in an up-flow packed bed reactor is presented. This paper presents an approximate analytical method (Modified adomian decomposition method) to solve the non-linear differential equations for Michaelis-Menten formalism that describe the concentrations of substrates within the enzymatic layer. A simple and closed-form of expressions pertaining to substrate concentration and effectiveness factor are presented for all value of diffusion parameters. These analytical results are compared with numerical results and they are found to be in good agreement.

Keywords*: Acetophenone, Packed bed reactor, Michaelis-Menten kinetics, Modified adomian decomposition method.*

1. INTRODUCTION:

For the past few years, one of the major focus area in biotechnology is biocatalysis. Chiral compounds, especially chiral alcohols has become a very important intermediates in the synthesis of enantiomerically pure pharmaceuticals. The need for optically active drugs has increased in pharmaceutical and agrochemical fields in the recent years. There are number of potential applications available for (*R*)-1-Phenylethanol or (*S*)-1-Phenylethanol which is used as a building blocks for the synthesis of bioactive compounds [1-6]. The enantioselective reduction of ketones was catalyzed by alcohol dehydrogenases (ADHs) for the synthesis of chiral alcohols with the help of nicotinamide cofactors (NADH or NADPH) [7]. Therefore, the asymmetric reduction of ketones to their corresponding alcohols is useful in organic synthesis. The enzyme purification and cofactor addition or the requirement for an associate system for cofactor regeneration should be avoided by using whole cells rather than isolated enzymes. One of the significant of using whole cells is that the whole reaction system for cofactor regeneration is present within the cell themselves. On the other hand, biotechnology opens up future prospects in the chemical field for the synthesis of complex compounds and combines inexpensive raw materials with environmentally friendly processes [8]. Microorganisms are generally much less expensive, and in some cases, enzymes are more stable within the cell, thus extending the life of the biocatalyst. Further, whole cells are easier to be obtained and cheaper than isolated enzymes [9-10]. While comparing, immobilized cell systems has more advantage than conventional suspended (free) cell systems. Kurbanoglu and co-workers [11] introduced a designed reactor for continuous production of (S)-1-phenylethanol by immobilized cells of Rhodotorula glutinis in calcium alginate gel. Hasegawa and co-workers [12] studied the bioreduction of acetophenone in calcium alginate immobilized Hansenula capsulate cells using a packed bed reactor.

Asymmetric bioreduction of acetophenone is accomplished by immobilized cells in this study. The use of immobilized whole cells in industrial processes has attracted considerable attention due to various advantages, such as an increase of conversion and cellular stability, and a decrease of procedure expenses due to the easy cell recovery and reutilization. Immobilization provides high cell concentration and cell reuse. However, mass transfer limitations are important when immobilized cells were used. To verify the effect of mass transfer limitations, effectiveness factor and observable modulus were obtained experimentally.

Recently, Aydogan et al [13]. evaluated the effectiveness factors and effective diffusion coeffients of acetophenone in κ-carrageenan gel. Also, Aydogan et al. [13] have reported the analysis of bioreduction of acetophenone, substrate diffusion, Michaelis-Menten rate equation, and chemical reaction in an up-flow packed bed reactor. However, to the best of our knowledge, there were no analytical results available till date that corresponds to the steady-state substrate concentration and effectiveness factor for all possible values of dimensionless parameters. Therefore, herein, we employ Modified adomian decomposition method to evaluate the steady-state substrate concentration and effectiveness factor for all possible values of dimensionless parameters γ and α. These parameters are defined in the Equation (6).

2. MATHEMATICAL FORMULATION OF THE NON LINEAR DIFFUSION EQUATION:

The rate of reaction determining processes to be assumed when analyzing the operation of a porous particle for the immobilized biocatalysis are: (i) microorganisms act as an enzyme stores, (ii) microorganisms is disturbed uniformly throughout the particle, (iii) transport of substrate through the catalyst is described by the Fick's law form relating the diffusive flux to the substrate concentration gradient, and the effective diffusivity of substrate is constant, (iv) electrostatic effects are negligible, and (v) the reaction kinetics. In this case, the steady – state kinetic constant of the reaction r is given by the Michaelis – Menten equation

$$r = \frac{r_{\max} C}{K_M + C} \tag{1}$$

where $r_{\max}$ is the maximum reaction rate , K_M is the Michaelis – Menten constant and, C is the concentration of substrate respectively. The diffusion equation for a spherical porous particle with a constant diffusion coefficient at steady state [14-15] is

$$D_e \left(\frac{d^2 C}{dr^2} + \frac{2}{r} \frac{dC}{dr} \right) = \frac{r_{\max} \mathrm{C}}{K_{\mathrm{M}} + C} \tag{2}$$

Here D_e is the effective diffusivity of substrate. The boundary conditions are

$$r = R;\ C = C_0 \tag{3}$$

$$r = 0; \frac{dC}{dr} = 0 \tag{4}$$

where R is the particle radius and C_0 is the bulk concentration of substrate. The definition of the effectiveness factor is given by [16]

$$\eta = \frac{4 \pi R^2 D_{\mathrm{e}} (dC/dr)_{r=R}}{(4/3) \pi R^3 (r_m C_0 / (K_M + C_0))} \tag{5}$$

We can assume that Equation (2) is transformed to dimensionless form using the following dimensionless variables

$$U = \frac{C}{C_0};\ \rho = \frac{r}{R};\ \gamma = \frac{r_{\max} R^2}{D_e K_M};\ \alpha = \frac{C_0}{K_M} \tag{6}$$

The diffusion equation (2) in dimensionless form is

$$\frac{d^2 U}{d\rho^2} + \frac{2}{\rho} \frac{dU}{d\rho} = \frac{\gamma U}{1 + \alpha U} \tag{7}$$

The boundary conditions in dimensionless forms are

$$\rho = 1;\ U = 1 \tag{8}$$

$$\rho = 0; \frac{dU}{d\rho} = 0 \tag{9}$$

The effectiveness factor (η) is given by

$$\eta = \frac{3(\alpha + 1)}{\gamma} \left(\frac{dU}{d\rho} \right)_{\rho = 0} \tag{10}$$

3. ANALYTICAL SOLUTION OF THE CONCENTRATION USING MODIFIED ADOMIAN DECOMPOSITION METHOD:

In the recent years, much attention is devoted to the application of the adomian decomposition method to the solution of various scientific models [17]. An efficient modification of the standard adomian decomposition method for solving singular initial value problem in the second order ordinary differential equation. The MADM yields, without linearization, perturbation, transformation or discretisation, an analytical solution in terms of a rapidly convergent infinite power series with easily computable terms. The decomposition method is simple and easy to use and produces reliable results with few iterations used. The results show that the rate of convergence of modified adomian decomposition method is higher than standard adomian decomposition method [18-22]. Using this method (see Appendix A), we can obtain the analytical expression of concentration (see Appendix B), of the substrate as follows:

$$U(\rho,\gamma,\alpha)=1-\frac{\gamma}{6(1+\alpha)}+\frac{7\gamma^2}{360(1+\alpha)^3}+\left(\frac{\gamma}{6(1+\alpha)}-\frac{\gamma^2}{36(1+\alpha)^3}\right)\rho^2+\frac{\gamma^2}{120(1+\alpha)^3}\rho^4 \tag{11}$$

Using Eq. (10), we can obtain the effectiveness factor

$$\eta(\gamma,\alpha)=1-\frac{\gamma}{15(1+\alpha)^2} \tag{12}$$

Provided $\gamma \le 15(1+\alpha)^2$. The Equation (11) and (12) represent the new and simple analytical expression of concentration of substrate and effectiveness factor of packed bed reactor.

4. NUMERICAL SIMULATION:

The diffusion equation (Equation 7) for the boundary conditions (Equations (8) and (9)) is also solved numerically. We have used the function pdex1 in MATLAB software to solve numerically the initial-boundary value problems for the nonlinear differential equations. This numerical solution is compared with our analytical results in Figures (1) and (2). Upon comparison, it gives a satisfactory agreement for all values of the dimensionless parameters, γ and α. The MATLAB program is also given in Appendix *C*.

5. DISCUSSION:

The kinetic response of a bioreactor depends on the concentration of substrate. The concentration of substrate depends on the following two factors γ and α. γ is the diffusion parameter, which represents the ratio of the characteristic time of the enzymatic reaction to that of substrate diffusion. The diffusion parameter γ can be varied by changing either the radius of the bioreactor or the amount of catalyst in packed bed reactor. This parameter describes the relative importance of diffusion and reaction in packed bed reactors. When γ is small, the kinetics are dominant resistance; the uptake of substrate in bioreactor is kinetically controlled. Under these conditions, the substrate concentration profile across the bioreactor is essentially uniform. The overall kinetics are determined by the total amount of active catalyst. When the parameter γ is large, diffusion limitations are the principal determining factor.

Figure 1(a)-(*d*) shows the dimensionless substrate concentration U versus dimensionless distance ρ in packed bed reactor for various values of the dimensionless parameters γ and α. From figure 1(a)-(d), it is evident that the value of concentration $U \approx 1$ when $\rho = 1$ and $\gamma \le 0.5$ for all values of α. The concentration differs significantly for all values of α and the value of the concentration U decreases when γ increases. In the normalized steady state substrate concentration U is plotted for all values of the dimensionless parameter γ in Figure 2(a)-(d). From Figure 2(a)-(d), it is evident that the normalized steady state substrate concentration U reaches the maximum value at $\rho = 1$ and $\gamma \le 1$. The substrate concentration differs significantly only when $\alpha \ge 5$ (see Figure 2(c) and (d)). The value of concentration U is directly proportional to the value of the parameter α. In all the cases the agreement between the simulation work and our analytical results is good.

The variation in effectiveness factor for various values of α, R and C_0 using Equation 12 is shown in Figures 3 and 4. From Figures 3(a)-(b), it is evident that the effectiveness factor increases with the increasing value of the dimensionless parameter α. Figures 3(c) indicates the effectiveness factor for small values of bulk concentration of substrate C_0 when $K_M = 0.37 \text{ mmol L}^{-1}$. From Figure3(c), it is concluded that the effectiveness factor increases when C_0 increases.

Also when $C_0 \geq 50\,\text{mmol}\,\text{L}^{-1}$, all the curves reach the steady-state value. Figure 4 represents the effectiveness factor η for various values of particle radius R. From the figure it is inferred that η decreases when R increases.

6. CONCLUSIONS:

In this work, we have presented a theoretical model describing the process of reaction and diffusion of a substrate accomplished by immobilized cells. We have obtained the transport and kinetics that are described in terms of the reaction/diffusion parameter α and γ. The approximate analytical expression for the steady state concentration of substrate for all values of α and γ in a packed bed reactor was obtained using the Modified adomian decomposition method. A satisfactory agreement with the numerical result is noted. Moreover, we have also presented a closed form expression for the effectiveness factor.

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Appendix A:

Consider the nonlinear differential equation in the form

$$y'' + \frac{2n}{x}y' + \frac{n(n-1)}{x^2}y + F(x,y) = g(x)\ ;\ n \geq 0 \tag{A.1}$$

with initial condition

$$y(0) = A,\ y'(0) = B$$

where $F(x,y)$ is a real function, $g(x)$ is the given function and A and B are constants. We propose the new differential operator, as below

$$L = x^{-n}\frac{d^2}{dx^2}x^n y \tag{A.2}$$

So, the problem (A.1) can be written as,

$$Ly = g(x) - F(x,y). \tag{A.3}$$

The inverse operator L^{-1} is therefore considered a two-fold integral operator, as below.

$$L^{-1}(.) = x^{-n}\int_0^x\int_0^x x^n\,(.)\,dx\,dx \tag{A.4}$$

Applying L^{-1} of (A.4) to the first three terms $y'' + \frac{2n}{x}y' + \frac{n(n-1)}{x^2}y$ of Equation (A.1) we find

$$L^{-1}\left(y'' + \frac{2n}{x}y' + \frac{n(n-1)}{x^2}y\right) = x^{-n}\int_0^x\int_0^x x^n\left(y'' + \frac{2n}{x}y' + \frac{n(n-1)}{x^2}y\right)dx\,dx$$

$$= x^{-n}\int_0^x (x^n y' + nx^{n-1}y)\,dx$$

$$= y - y(0)$$

By operating L^{-1} on (A.3), we have

$$y(x) = A + L^{-1}g(x) - L^{-1}F(x,y) \tag{A.5}$$

The Adomian decomposition method introduce the solution $y(x)$ and the nonlinear function $F(x,y)$ by infinity series

$$y(x) = \sum_{n=0}^{\infty} y_n(x), \tag{A.6}$$

And

$$F(x, y) = \sum_{n=0}^{\infty} A_n \tag{A.7}$$

where the components $y_n(x)$ of the solution $y(x)$ will be determined recurrently and the Adomian polynomials A_n of $F(x, y)$ are evaluated [23-25] using the formula

$$A_n(x) = \frac{1}{n!}\frac{d^n}{d\lambda^n} N\left(\sum_{n=0}^{\infty}(\lambda^n y_n)\right)|_{\lambda=0} \tag{A.8}$$

By substituting (A.6) and (A.7) into (A.5),

$$\sum_{n=0}^{\infty} y_n(x) = A + L^{-1}g(x) - L^{-1}\sum_{n=0}^{\infty} A_n \tag{A.9}$$

Through using Adomian decomposition method, the components $y_n(x)$ can be determined as

$$\begin{aligned} y_0(x) &= A + L^{-1}g(x) \\ y_{n+1}(x) &= -L^{-1}(A_n), n \geq 0 \end{aligned} \tag{A.10}$$

which gives

$$\begin{aligned} y_0(x) &= A + L^{-1}g(x) \\ y_1(x) &= -L^{-1}(A_0) \\ y_2(x) &= -L^{-1}(A_1) \\ y_3(x) &= -L^{-1}(A_2) \\ &\ldots \end{aligned} \tag{A.11}$$

From (A.8) and (A.11), we can determine the components $y_n(x)$, and hence the series solution of $y(x)$ in (A.6) can be immediately obtained.

Appendix B:

In this appendix, we derive the general solution of nonlinear equation (7) by using Adomian decomposition method. We write the Equation (7) in the operator form,

$$L(U) = \frac{\gamma U}{1+\alpha U} \tag{B.1}$$

where $L = \rho^{-1}\frac{d^2}{d\rho^2}\rho$. Applying the inverse operator L^{-1} on both sides of Equation (B.1) yields

$$U(\rho) = A\rho + B + \gamma L^{-1}\left(\frac{U}{1+\alpha U}\right) \tag{B.2}$$

where *A* and *B* are the constants of integration. We let,

$$U(\rho) = \sum_{n=0}^{\infty} U_n(\rho) \tag{B.3}$$

$$N[U(\rho)] = \sum_{n=0}^{\infty} A_n \tag{B.4}$$

where $N[U(\rho)] = \left(\frac{U}{1+\alpha U}\right)$ (B.5)

In view of Equations (B. 3), (B. 4) and (B. 5), Eq. (B. 2) gives

$$\sum_{n=0}^{\infty} U_n(\rho) = A\,\rho + B + \gamma L^{-1} \sum_{n=0}^{\infty} A_n \tag{B.6}$$

We identify the zeroth component as

$$U_0(\rho) = A\,\rho + B \tag{B.7}$$

and the remaining components as the recurrence relation

$$U_{n+1}(\rho) = \gamma L^{-1} A_n \quad ; \quad n \geq 0 \tag{B.8}$$

where A_n are the Adomian polynomials of $U_1, U_2, ..., U_n$. We can find the first few A_n as follows:

$$A_0 = N(U_0) = \frac{1}{1+\alpha} \tag{B.9}$$

$$A_1 = \frac{d}{d\lambda}\left[N(U_0 + \lambda U_1)\right] = \frac{U_1}{(1+\alpha)^2} \tag{B.10}$$

The remaining polynomials can be generated easily, and so,

$$U_0 = 1 \tag{B.11}$$

$$U_1 = -\frac{\gamma}{6(1+\alpha)} + \frac{\gamma}{6(1+\alpha)}\rho^2 \tag{B.12}$$

$$U_2 = \frac{7\gamma^2}{360(1+\alpha)^3} - \frac{\gamma^2}{36(1+\alpha)^3}\rho^2 + \frac{\gamma^2}{120(1+\alpha)^3}\rho^4 \tag{B.13}$$

Adding (B. 11) to (B. 13) we get Equation (11) in the text.

Appendix C:

The Matlab program to find the numerical solution of Equation 8 is as follows.

```
function pdex1
m = 2;
x = linspace(0,1);
t = linspace(0,10000);
sol = pdepe(m,@pdex1pde,@pdex1ic,@pdex1bc,x,t);
% Extract the first solution component as u.
u = sol (:,:,1);
figure
plot(x,u(end,:))
xlabel('Distance x')
ylabel('u(x,2)')
% ---------------------------------------------------------------
function [c,f,s] = pdex1pde(x,t,u,DuDx)
c = 1;
f = DuDx;
r=0.1;
a=0.1;
s =-(r*u)/((1+(u*a)));
% ---------------------------------------------------------------
pl = 0;
ql = 1;
pr = ur-1;
qr = 0;
```

Appendix D:

Nomenclature

r_{max} maximum reaction rate (mmol L^{-1} min^{-1})
K_M Michaelis-Menten constant (mmol L^{-1})
C substrate concentration in gel (mmol L^{-1})
C_0 substrate concentration in bulk (mmol L^{-1})
r radial distance (cm)
R particle radius (cm)
D_e effective diffusivity of substrate (cm^2/s)
U dimensionless substrate concentration

Greek letters:

α dimensionless Michaelis-Menten constant
η effectiveness factor
ρ dimensionless radial distance

Figures:

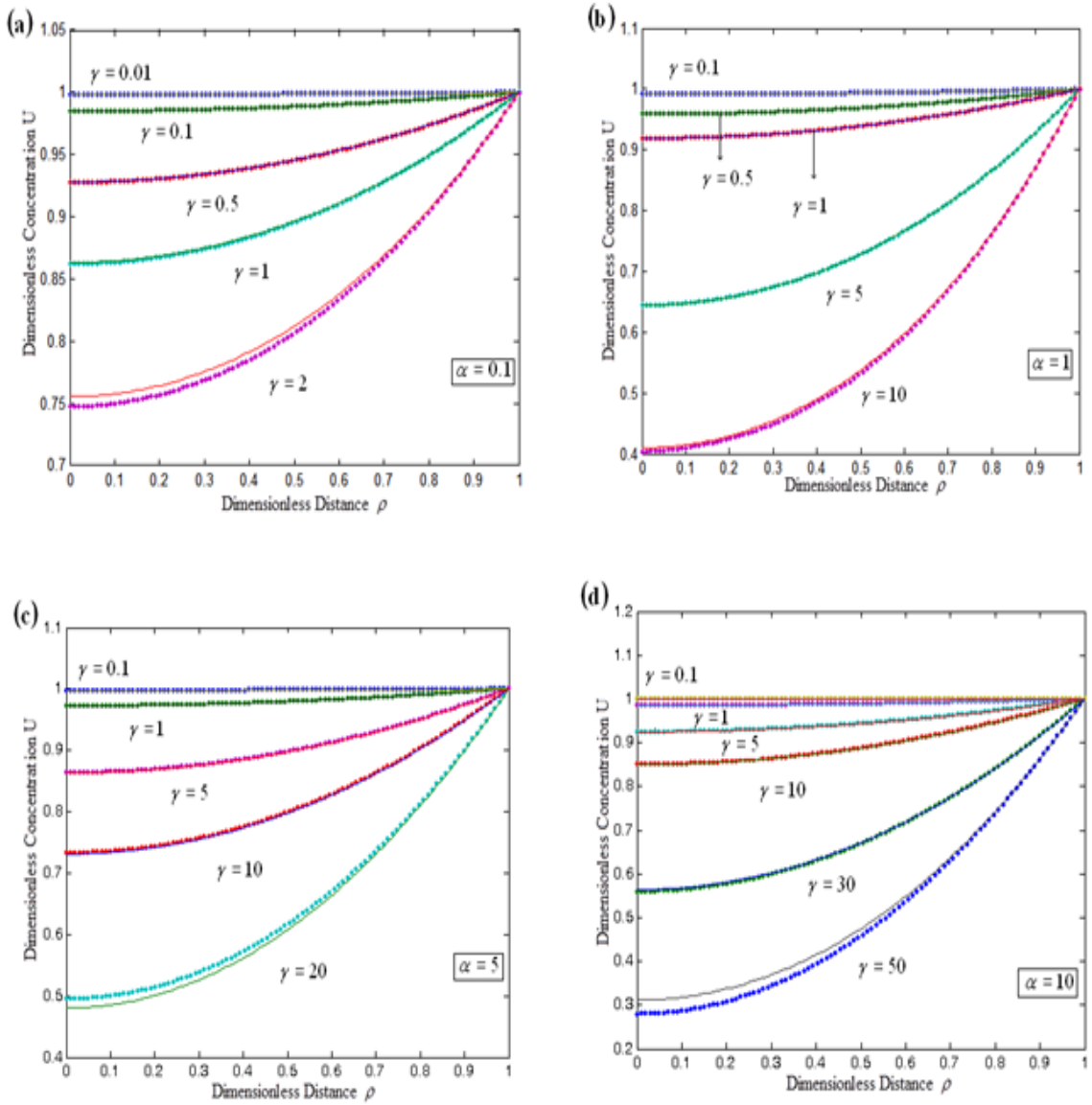

Figure-1: Plot of dimensionless substrate concentration U versus dimensionless distance ρ. The concentrations were computed for various values of the dimensionless parameter γ when (*a*) $\alpha = 0.1$, (*b*) $\alpha = 1$, (*c*) $\alpha = 5$, and (*d*) $\alpha = 10$.

The curves are plotted using Equation (12). (—) denotes the analytical results and (• • •) denotes the numerical simulations.

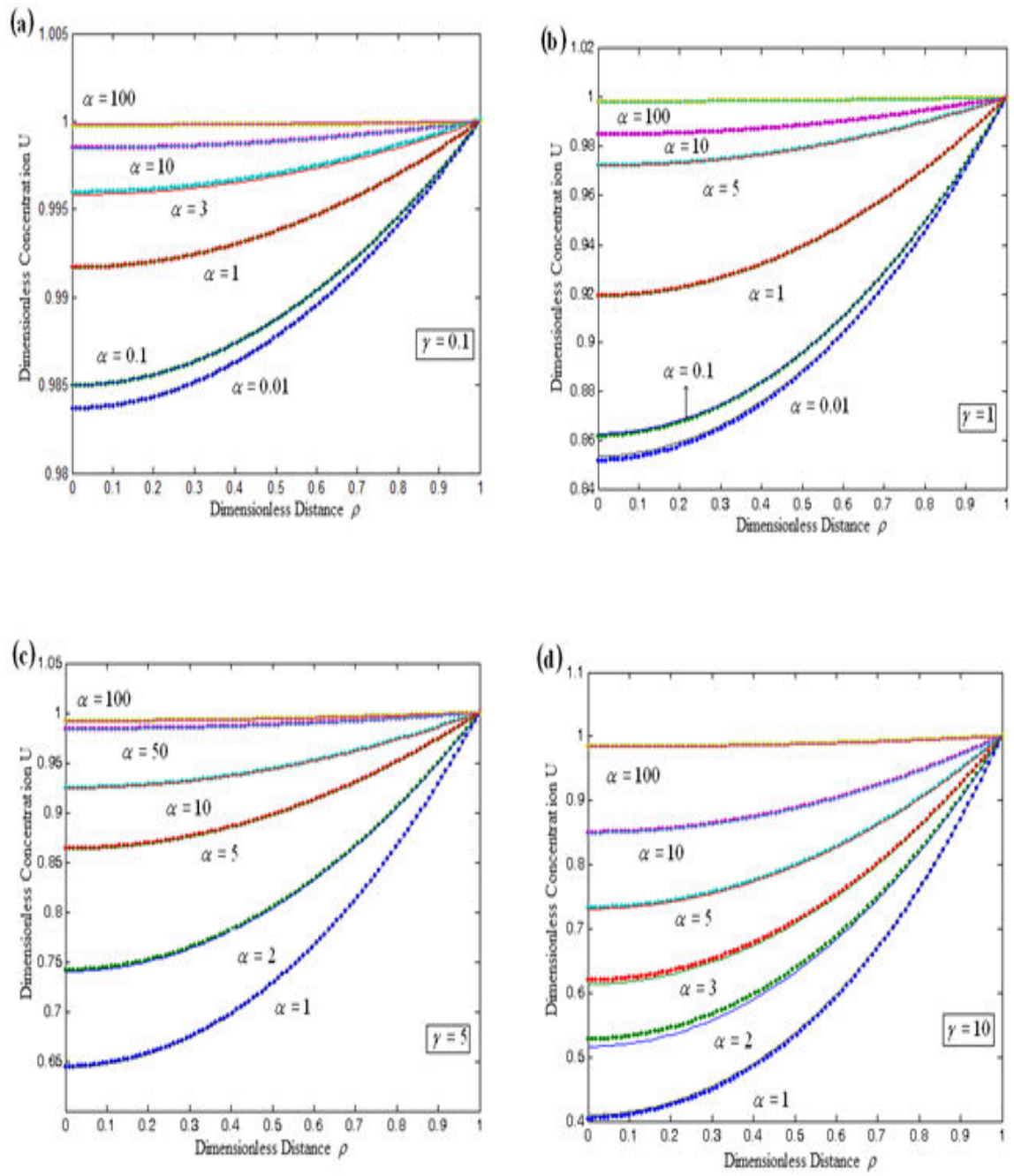

Figure-2: Plot of dimensionless substrate concentration U versus dimensionless distance ρ. The concentrations were computed for various values of the dimensionless parameter α when $(a)\ \gamma = 0.1$, $(b)\ \gamma = 1, (c)\ \gamma = 5$, and $(d)\ \gamma = 10$. The curves are plotted using Equation (12). (—) denotes the analytical results and (• • •) denotes the numerical simulations.

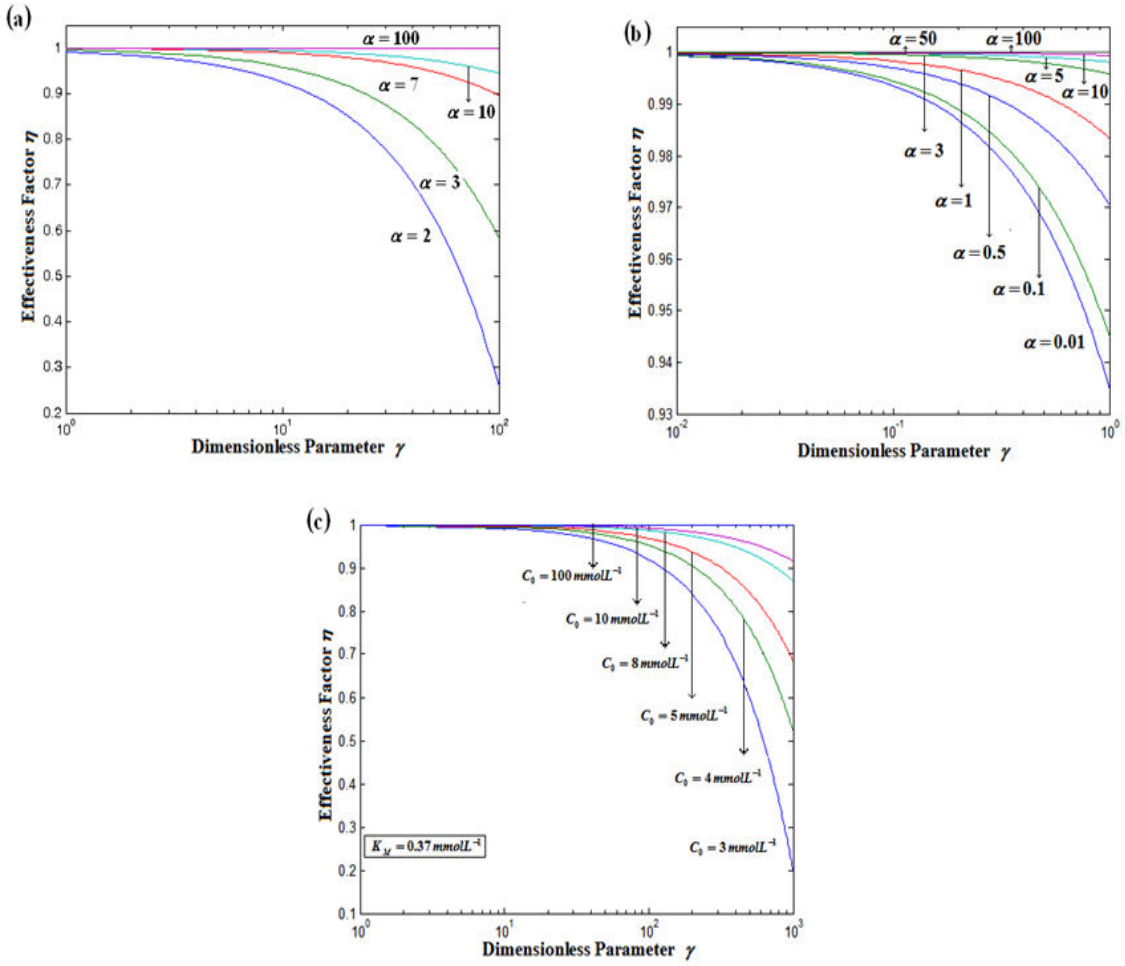

Figure-3: Plot of the effectiveness factor η versus dimensionless parameter γ. The effectiveness factor η were computed using Equation (13) when $(a)\,\alpha \geq 2$ and (b) $\alpha \geq 0.01$ and (c) $K_M = 0.37\ \text{mmolL}^{-1}$ for various values of the bulk concentration of substrate C_0.

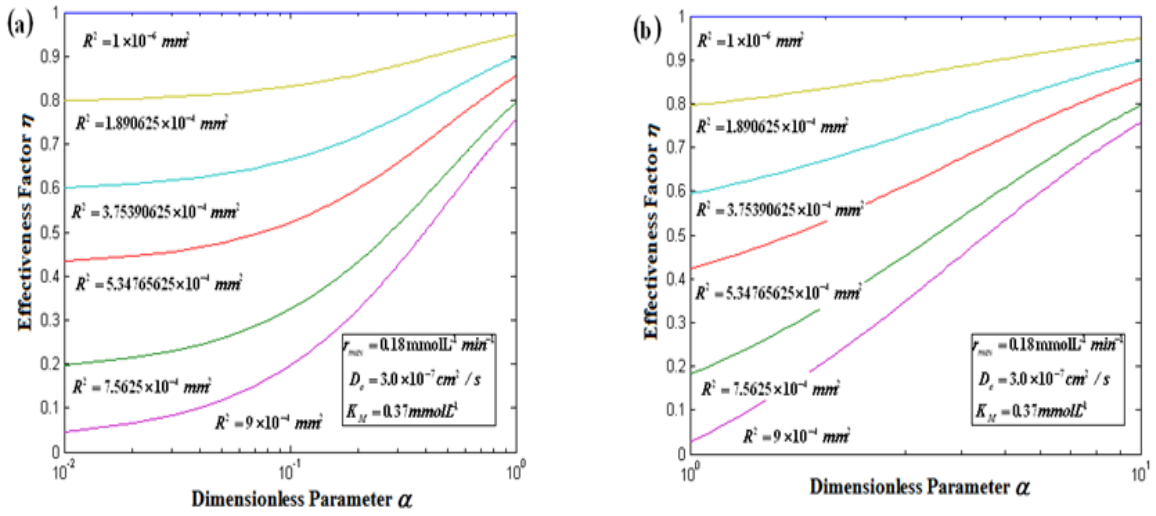

Figure-4: Plot of the effectiveness factor η versus dimensionless parameter α. The effectiveness factor η were computed using Equation (13) when $r_{\max} = 0.18\ \text{mmol L}^{-1}\ \text{min}^{-1}$, $K_M = 0.37\ \text{mmol L}^{-1}$ and $D_e = 3.0\times10^{-7}\ \text{cm}^2/\text{s}$ for various values of particle radius R.

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