

Fractional Dynamics of Infectious Disease Transmission with Optimal Control

Reza Akbari and Leader Navaei*

Abstract

This article investigates and studies the dynamics of infectious disease transmission using a fractional mathematical model based on Caputo fractional derivatives. Consequently, the population studied has been divided into four categories: susceptible, exposed, infected, and recovered. The basic reproduction rate, existence, and uniqueness of disease-free as well as infected steady-state equilibrium points of the mathematical model have been investigated in this study. The local and global stability of both equilibrium points has been investigated and proven by Lyapunov functions. Vaccination and drug therapy are two controllers that may be used to control the spread of diseases in society, and the conditions for the optimal use of these two controllers have been prescribed by the principle of Pontryagin's maximum. The stated theoretical results have been investigated using numerical simulation. The numerical simulation of the fractional optimal control problem indicates that vaccination of the susceptible subjects in the community reduces horizontal transmission while applying drug control to the infected subjects reduces vertical transmission. Furthermore, the simultaneous use of both controllers is much more effective and leads to a rapid increase in the cured population and it prevents the disease from spreading and turning into an epidemic in the community.

Keywords: Fractional calculus, Infectious disease, Optimal control.

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*Corresponding author (E-mail: r.akbari@pnu.ac.ir)

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1. Introduction

Diseases have always played an important role in human history. Infectious diseases have had a significant impact on population growth, progress in wars, and the economy of countries (such as the plague in the 14th century or the COVID-19 virus in the current century). Despite the existence of extensive preventive and therapeutic measures, including improvements in public health, antibiotics, and vaccination, infectious diseases are still the leading cause of death from diseases in societies. Infectious pathogens (which include bacteria, fungi, protozoa, worms, viruses) are sometimes so adapted to new conditions and even mutated that they cause the reappearance and emergence of new infections (such as hepatitis C, hepatitis E, and AIDS). Hence, the dynamics of infectious disease transmission, the spread of these diseases, and the methods of controlling them have received attention in recent years.

The spread and progress of the disease in a society may lead to a division among people of that society into different groups depending on their status in the ability to transmit the disease to others. Susceptible individuals are those who do not have a disease but can get sick. Those who are exposed to the disease or in the incubation period are the ones who act like the host of the disease but are not yet able to transmit it. The infected individuals are those who have a disease and can transmit it to healthy ones. Also, the recovered ones are those who have recovered from the disease. Usually, these population groups are represented by symbols S, E, I, and R, respectively. There are several mathematical models for disease dynamics, depending on the number and type of compartments. For example, *SIS*, *SIR*, *SIRS*, and *SEIR* models, which represent stages of the disease for each individual in a population [1–3].

Accordingly, more realistic mathematical models for studying disease outbreaks are an important tool to investigate this issue. Mathematical models of disease outbreaks, which are usually called epidemic models, are often expressed in terms of ordinary differential equations, and partial differential equations. But due to the ability of fractional calculus to model and describe the dynamics of real-world processes with special features, many mathematicians have tried to model real processes using fractional calculus. Hence, some researchers have extended classical epidemic models to fractional-order epidemic systems.[4–11].

In most of the researches, mortality from the disease is not considered, but in this proposed model, death due to disease and natural death are considered separately. Also, in the proposed model, there are coefficients for controls that check the effect of controls, which in most of the researches these coefficients are not seen.

Considering the above-stated explanation, this article suggested and reviewed a fractional-order mathematical model using the Caputo fractional derivative of order α , for the dynamics of infectious disease transmission with two control mechanisms, vaccination and drug therapy, to investigate the spread of infectious diseases and the method for optimally control it in society. In this model, infectious dis-

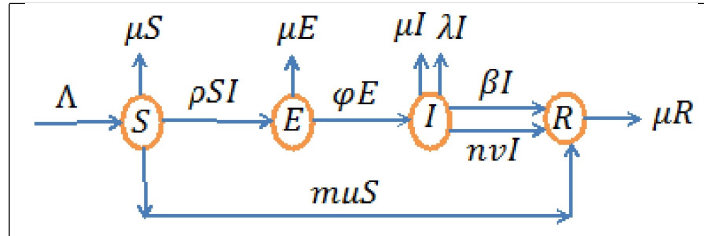


Figure 1: Schematic diagram of the model (1).

ease can be transmitted through two ways including direct contact with an infected person (horizontal transmission) and transfer from parent to child (transmission of infection from mother to fetus during prenatal, intra or postnatal period) (vertical transmission). The present study examines optimal strategies for optimally controlling the spread of the disease in society using optimal control theory. Also, the optimal conditions of the fractional control of the spread of infectious diseases in society have been stated using the principle of Pontryagin’s maximum. Also, the simultaneous use of both controllers is much more effective and leads to a rapid increase in the cured population and prevents the disease from spreading and becoming an epidemic in the community.

The remainder of the paper is structured as follows. In Section 2, we present the fractional *SEIR* mathematical model for infectious disease transmission. In Section 3, the existence, as well as uniqueness, of the equilibrium points and their local and global asymptotic stability of the equilibrium points are studied. In Section 4, the optimal control problem will be defined and studied. In Section 5, we will show the numerical results with a numerical example. Finally, in Section 6 the paper is closed with some conclusions.

2. Fractional-order model formulation

In this section, we present a fractional-order *SEIR* model in the sense of *Caputo*. The total host population, $N(t)$ is divided into four classes namely Suspected ($S(t)$), Exposed ($E(t)$), Infected ($I(t)$), and Recovered ($R(t)$).

$$\begin{cases} {}^C\mathcal{D}_{0^+}^\alpha S(t) = \Lambda - \rho S(t)I(t) - (\mu + mu)S(t), \\ {}^C\mathcal{D}_{0^+}^\alpha E(t) = \rho S(t)I(t) - (\phi + \mu)E(t), \\ {}^C\mathcal{D}_{0^+}^\alpha I(t) = \phi E(t) - (\mu + \lambda + \beta + nv)I(t), \\ {}^C\mathcal{D}_{0^+}^\alpha R(t) = muS(t) + (\beta + nv)I(t) - \mu R(t), \end{cases} \quad (1)$$

$$S(0) \geq 0, E(0) \geq 0, I(0) \geq 0, R(0) \geq 0.$$

A flow chart of this compartmental model is shown in [Figure 1](#). In these equations, all the parameters are nonnegative. Since $R(t)$ does not appear in the first three

Table 1: The parameters of the model and their descriptions.

Symbol	Description	Values range	Reference
μ	Rate of death population	0.002	[12]
Λ	Recruitment rate	0.0121	[12]
ρ	Transmission coefficient	0.125	[13]
ϕ	Rate moving from E to I	0.02	[14]
β	Rate moving from I to R without antiviral drug	0.025	[13]
λ	Rate of death population by infectious disease	0.0008	[13]
u	Vaccination rate	$0 \leq u \leq 1$	-
v	Antiviral drug rates	$0 \leq v \leq 1$	-
m	Vaccine efficacy	0.81	[15]
n	Efficacy of the drug	0.71	[15]

equations of system (1), without loss of generality we discuss the following system:

$$\begin{cases} {}^C\mathcal{D}_{0+}^\alpha S(t) = \Lambda - \rho S(t)I(t) - (\mu + mu)S(t), \\ {}^C\mathcal{D}_{0+}^\alpha E(t) = \rho S(t)I(t) - (\phi + \mu)E(t), \\ {}^C\mathcal{D}_{0+}^\alpha I(t) = \phi E(t) - (\mu + \lambda + \beta + nv)I(t), \\ S(0) \geq 0, E(0) \geq 0, I(0) \geq 0. \end{cases} \quad (2)$$

At any time t , we have $R(t) = N(t) - S(t) - E(t) - I(t)$. In the next section, we investigate the existence and stability conditions of both equilibriums of system (2), by constructing appropriate Lyapunov functionals.

3. Stability of equilibria

To investigate the existence, uniqueness and non-negativity of the solution and stability of the equilibrium points of system (2), we consider the following theorem:

Theorem 3.1. *System (2) has a unique solution. Furthermore, all components of the solution are non-negative.*

Proof. The existence and uniqueness of the solution follows from Theorem 2.1 and 3.1 of [16], respectively. To show the nonnegativity of the solution, from second equation of system (2), we obtain:

$${}^C\mathcal{D}_{0+}^\alpha E(t) = \rho S(t)I(t) - (\phi + \mu)E(t) \geq -(\phi + \mu)E(t).$$

Therefore,

$$E(t) \geq E_{\alpha, \alpha+1}(-(\phi + \mu)t^\alpha)E(0) \geq 0. \quad (3)$$

From the third equation of system (2), we obtain:

$${}^C\mathcal{D}_{0+}^\alpha I(t) = \phi E(t) - (\mu + \lambda + \beta + nv)I(t) \geq -(\mu + \lambda + \beta + nv)I(t).$$

Then

$$I(t) \geq E_{\alpha, \alpha+1}(-(\mu + \lambda + \beta + nv)t^\alpha)I(0) \geq 0. \tag{4}$$

According to system (2), (3) and (4) we get easily:

$$\begin{aligned} {}^C\mathcal{D}_{0+}^\alpha S(t)|_{S=0} &= \Lambda \geq 0, \\ {}^C\mathcal{D}_{0+}^\alpha E(t)|_{E=0} &= \rho S(t)I(t) \geq 0, \\ {}^C\mathcal{D}_{0+}^\alpha I(t)|_{I=0} &= \phi E(t) \geq 0. \end{aligned}$$

From $(S(0), E(0), I(0)) \in \mathbb{R}_+^3$ and Lemma 2.2 of [17], we received the required result i.e. $S(t), E(t), I(t) \geq 0$ for any $t \geq 0$. Then the solution of system (2), will lie in \mathbb{R}_+^3 .

Now, we show that the solution of system (2) is bounded. Define a function

$$M(t) = S(t) + E(t) + I(t).$$

Then

$${}^C\mathcal{D}_{0+}^\alpha M(t) = {}^C\mathcal{D}_{0+}^\alpha S(t) + {}^C\mathcal{D}_{0+}^\alpha E(t) + {}^C\mathcal{D}_{0+}^\alpha I(t).$$

Adding all equations of system (2):

$${}^C\mathcal{D}_{0+}^\alpha M(t) \leq \Lambda - \mu M(t).$$

Applying the Laplace transform in the previous inequality, we get:

$$s^\alpha L(M) - s^{\alpha-1}M(0) \leq \Lambda s^{-1} - \mu L(M).$$

Then

$$M(t) \leq \Lambda t^\alpha E_{\alpha, \alpha+1}(-\mu t^\alpha) + E_{\alpha, 1}(-\mu t^\alpha)M(0),$$

where $E_{\alpha, \beta}(z)$ is the Mittag-Leffler function. Let $K = \max\{\Lambda, M(0)\}$, so

$$M(t) \leq K[\mu t^\alpha E_{\alpha, \alpha+1}(-\mu t^\alpha) + E_{\alpha, 1}(-\mu t^\alpha)] = K \frac{1}{\Gamma(1)} = K.$$

Then, the solution of system (2) is bounded. □

Therefore, we conclude that the feasible region of system (2) is given by

$$\Omega = \{(S, E, I) \in \mathbb{R}^3 \mid S > 0, E \geq 0, I \geq 0 \text{ and } S + E + I \leq K\}.$$

Theorem 3.2. *The model (2) has at most two equilibrium points:*

- a. A disease free equilibrium $\mathcal{E}_f = (S_0, E_0, I_0) = (\frac{\Lambda}{\mu+mu}, 0, 0)$;

b. A infected steady-state equilibrium: $\mathcal{E}_e = (S^*, E^*, I^*)$, where

$$\begin{aligned} S^* &= \frac{(\mu + \lambda + \beta + nv)(\phi + \mu)}{\rho\phi}, \\ E^* &= \frac{\rho\phi\Lambda - (\mu + \lambda + \beta + nv)(\mu + mu)(\phi + \mu)}{\rho\phi(\phi + \mu)}, \\ I^* &= \frac{\rho\phi\Lambda - (\mu + \lambda + \beta + nv)(\mu + mu)(\phi + \mu)}{\rho(\phi + \mu)(\mu + \lambda + \beta + nv)}. \end{aligned}$$

In according with the concept of basic reproduction number R_0 in [18], (Figure 2), we have:

$$F = \begin{bmatrix} 0 & \rho S_0 \\ \phi & 0 \end{bmatrix}, \quad V = \begin{bmatrix} \phi + \mu & 0 \\ 0 & \mu + \lambda + \beta + nv \end{bmatrix}.$$

The reproduction number is given by:

$$R_0 = \rho(FV^{-1}),$$

where $\rho(FV^{-1})$ denotes the spectral radius of a matrix FV^{-1} . Then

$$R_0 = \frac{\rho\phi\Lambda}{(\mu + \lambda + \beta + nv)(\mu + mu)(\mu + \phi)}.$$

According to system (2) and by simple calculation, we get the following result:

Theorem 3.3. *The equilibrium \mathcal{E}_f of system (2) is locally asymptotically stable if, $R_0 < 1$.*

Proof. According to Lemma 3 of [19], determining the Jacobian matrix of the fractional system (2), at E_f we have:

$$J = \begin{bmatrix} -(\mu + mu) & 0 & -\frac{\rho\Lambda}{\mu + mu} \\ 0 & -(\phi + \mu) & \frac{\rho\Lambda}{\nu + mu} \\ 0 & \phi & -(\mu + \lambda + \beta + nv) \end{bmatrix}.$$

Thus

$$\text{tr}(J) = -[3\mu + mu + nv + \phi + \lambda + \beta] < 0,$$

and

$$\det(J) = -[(\mu + mu)(\phi + \mu)(\mu + \lambda + \beta + nv) - \rho\phi\Lambda] < 0.$$

The second compound [20] of the Jacobian matrix is

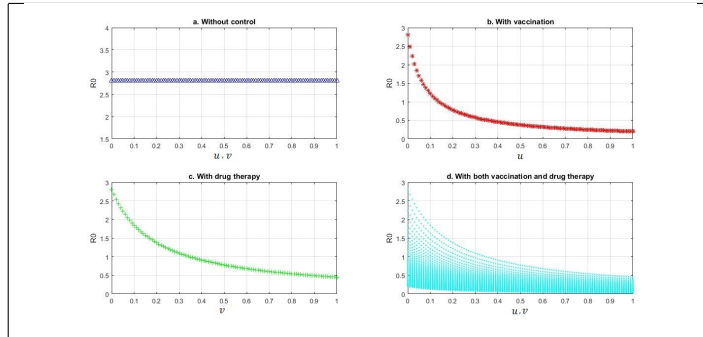


Figure 2: The behavior of R_0 both with control and without control.

$$J^{[2]} = \begin{bmatrix} J_{1,1}^{[2]} & \frac{\rho\Lambda}{\mu+mu} & \frac{\rho\Lambda}{\mu+mu} \\ \phi & J_{2,2}^{[2]} & 0 \\ 0 & 0 & J_{3,3}^{[2]} \end{bmatrix},$$

where

$$\begin{aligned} J_{1,1}^{[2]} &= -(2\mu + \phi + mu), \\ J_{2,2}^{[2]} &= -(2\mu + mu + nv + \lambda + \beta), \\ J_{3,3}^{[2]} &= -(2\mu + \phi + \lambda + \beta + nv). \end{aligned}$$

The determinant of this is

$$\det(J^{[2]}) = -(2\mu + \phi + \lambda + \beta + nv) \left[(2\mu + mu + \phi)(2\mu + mu + nv + \lambda + \beta) - \frac{\rho\phi\Lambda}{\mu + mu} \right] < 0.$$

Thus, $tr(J)$, $\det(J)$ and $\det(J^{[2]})$ are all negative. Therefore, by Lemma 3 of [19], all the eigenvalues of J have a negative real part. Thus, according to Theorem 4.3 of [21], the disease-free equilibrium at \mathcal{E}_f of a model (2), will be locally asymptotically stable if, $R_0 < 1$. \square

Theorem 3.4. For system (2) the equilibrium \mathcal{E}_e is globally asymptotically stable if, $R_0 > 1$.

Proof. For the equilibrium \mathcal{E}_e we define the following Lyapunov function:

$$V(t) = S^* g\left(\frac{S(t)}{S^*}\right) + E^* g\left(\frac{E(t)}{E^*}\right) + \frac{\phi + \mu}{\phi} I^* g\left(\frac{I(t)}{I^*}\right),$$

where $g(x) = x - 1 - \ln x$.

For all $S(t) > 0$, $E(t) > 0$ and $I(t) > 0$, V is well-defined, continuous and positive definite. According to Lemma 3.1 of [3], one gets

$$\begin{aligned} {}^C\mathcal{D}_{0+}^\alpha V(t) &\leq \left(1 - \frac{S^*}{S(t)}\right) {}^C\mathcal{D}_{0+}^\alpha(S) + \left(1 - \frac{E^*}{E(t)}\right) {}^C\mathcal{D}_{0+}^\alpha(E) + \frac{\phi + \mu}{\phi} \left(1 - \frac{I^*}{I(t)}\right) {}^C\mathcal{D}_{0+}^\alpha(I) \\ &= -(\mu + mu) \frac{(S - S^*)^2}{S} - \rho S^* I^* \left[g \left(\frac{S^*}{S(t)} \right) + g \left(\frac{S(t)I(t)E^*}{S^*I^*E(t)} \right) + g \left(\frac{E(t)I^*}{E^*I(t)} \right) \right]. \end{aligned}$$

Thus if $R_0 > 1$, it follows that ${}^C\mathcal{D}_{0+}^\alpha V(t)$ is negative definite. Therefore, the infected steady-state \mathcal{E}_e is globally asymptotically stable. \square

4. Optimal vaccination and drug therapy

The previous part examined the asymptotic stability of DFE and EE equilibrium points under the conditions for system (1) parameters. Applying vaccination and drug therapy to control the disease in society introduces societal costs. These costs can be either material or moral. Vaccination costs include purchasing and maintaining vaccines, as well as potential side effects. Drug therapy costs encompass medication, hospitalization, testing, and potential treatment side effects. Our duty is to optimize these costs. The best and most useful tool to achieve this goal is the definition of an optimal control problem, which will create limitations for the parameters of the problem. Hence, we define a control set as follows:

$$\mathcal{U} = \left\{ (u(t), v(t)) \mid 0 \leq u(t) \leq u_{\max}(t) \leq 1, 0 \leq v(t) \leq v_{\max}(t) \leq 1, t \in [0, t_f] \right\},$$

while the control set \mathcal{U} is Lebesgue measurable.

$$J(u, v) = \min_{u, v \in \mathcal{U}} \mathcal{I}_{t_f}^\alpha [AI(t) + \frac{1}{2}(C_1 u^2 + C_2 v^2)] dt \quad (5)$$

s.t :

$$\begin{cases} {}^C\mathcal{D}_{0+}^\alpha S(t) = \Lambda - \rho S(t)I(t) - (\mu + mu)S(t), \\ {}^C\mathcal{D}_{0+}^\alpha E(t) = \rho S(t)I(t) - (\phi + \mu)E(t), \\ {}^C\mathcal{D}_{0+}^\alpha I(t) = \phi E(t) - (\mu + \lambda + \beta + nv)I(t), \\ S(0) \geq 0, E(0) \geq 0, I(0) \geq 0. \end{cases}$$

Here, t_f is the final time and A is a positive weight to keep a balance in the size of infected population, C_1, C_2 describe the costs associated with vaccination and treatment respectively. The square of the disease control parameter is taken to remove some unwanted side effects of the disease as well as to consider the overdoses of the control [22]. Our goal is to minimize the objective function (5), that is, we need to seek the optimal control function $(u^*(t), v^*(t)) \in \mathcal{U}$ satisfying

$$J(u^*, v^*) = \min_{u, v \in \mathcal{U}} J(u, v).$$

The existence of an optimal control pair is guaranteed by the compactness of the control and the states spaces, and the convexity in the problem based on Theorem 4.1 in [23]. For optimality conditions, first, we find the Lagrangian and Hamiltonian for the problem (5). In fact, Lagrangian and Hamiltonian are defined by

$$L(I(t), u(t), v(t)) = AI(t) + \frac{1}{2}(C_1u^2 + C_2v^2),$$

and

$$\begin{aligned} & H(S(t), E(t), I(t), u(t), v(t), \lambda_1, \lambda_2, \lambda_3, t) \\ &= L(I(t), u(t), v(t)) + \lambda_1^C \mathcal{D}_{0+}^\alpha S(t) \\ &+ \lambda_2^C \mathcal{D}_{0+}^\alpha E(t) + \lambda_3^C \mathcal{D}_{0+}^\alpha I(t) \\ &= [AI(t) + \frac{1}{2}(C_1u^2 + C_2v^2)] \\ &+ \lambda_1(\Lambda - \rho S(t)I(t) - (\mu + mu)S(t)) \\ &+ \lambda_2(\rho S(t)I(t) - (\phi + \mu)E(t)) \\ &+ \lambda_3(\phi E(t) - (\mu + \lambda + \beta + nv)I(t)), \end{aligned}$$

where $\lambda_k, k = 1, 2, 3$ are the adjoint variables, which are determined by solving the following equations:

$$\begin{aligned} {}^C \mathcal{D}_{0+}^\alpha \lambda_1(t) &= -\frac{\partial H}{\partial S} = \lambda_1(\rho I(t) + \mu + mu) - \lambda_2 \rho I(t), \\ {}^C \mathcal{D}_{0+}^\alpha \lambda_2(t) &= -\frac{\partial H}{\partial E} = \lambda_2(\phi + \mu) - \lambda_3 \phi, \\ {}^C \mathcal{D}_{0+}^\alpha \lambda_3(t) &= -\frac{\partial H}{\partial I} = -A + \lambda_1 \rho S(t) - \lambda_2 \rho S(t) + \lambda_3(\mu + \lambda + \beta + nv), \end{aligned}$$

and the transversal conditions

$$\lambda_k(t_f) = 0 \quad k = 1, 2, 3.$$

By using Pontryagin minimum principle, we can obtain the optimal conditions as follows:

$$\frac{\partial H}{\partial u} = 0, \quad \frac{\partial H}{\partial v} = 0.$$

Then,

$$u^* = \min\{\max\{0, \frac{\lambda_1 m S^*}{C_1}\}, u_{\max}\}, \quad v^* = \min\{\max\{0, \frac{\lambda_3 n I^*}{C_2}\}, v_{\max}\}.$$

The above analysis can be expressed as the following theorem:

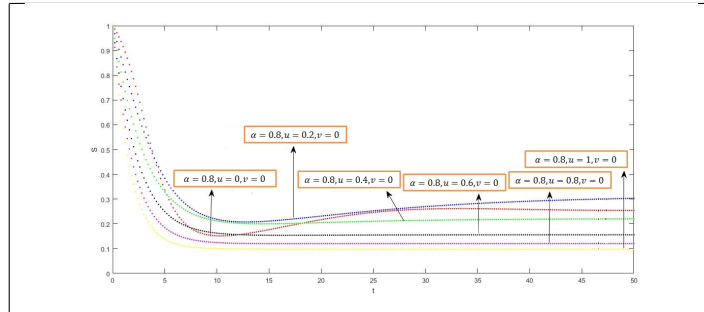


Figure 3: The behavior of S both with control and without control.

Theorem 4.5. Let (S^*, E^*, I^*) be the optimal state solution related to the optimal controls (u^*, v^*) for the optimal control problem (5). Then there exist adjoint variables λ_k ($k = 1, 2, 3$) that satisfy the following adjoint system:

$$\begin{aligned} {}^C\mathcal{D}_{0+}^\alpha \lambda_1(t) &= -\frac{\partial H}{\partial S} = \lambda_1(\rho I(t) + \mu + mu) - \lambda_2 \rho I(t), \\ {}^C\mathcal{D}_{0+}^\alpha \lambda_2(t) &= -\frac{\partial H}{\partial E} = \lambda_2(\phi + \mu) - \lambda_3 \phi, \\ {}^C\mathcal{D}_{0+}^\alpha \lambda_3(t) &= -\frac{\partial H}{\partial I} = -A + \lambda_1 \rho S(t) - \lambda_2 \rho S(t) + \lambda_3(\mu + \lambda + \beta + nv). \end{aligned}$$

with transversally conditions

$$\lambda_k(t_f) = 0, \quad k = 1, 2, 3.$$

Moreover, the optimal controls (u^*, v^*) which minimizes the problem (5) over the region \mathcal{U} can be shown as following:

$$u^* = \min \left\{ \max \left\{ 0, \frac{\lambda_1 m S^*}{C_1} \right\}, u_{\max} \right\}, \quad v^* = \min \left\{ \max \left\{ 0, \frac{\lambda_3 n I^*}{C_2} \right\}, v_{\max} \right\}.$$

5. Numerical results and discussion

In this section, we will discuss control problem (5) numerically and the values of defined parameters are shown in Table 1. To investigate the problem, we will consider two different situations including with and without control. The Runge-Kutta method of order 4 (RK4) is employed to solve the problem. The results are as follows:

Based on Figure 3, the susceptible population will decrease if the control and vaccination increase and as a result, the infected population will also decrease, and with the passage of time and the continuation of vaccination, horizontal transmission will dramatically decrease.

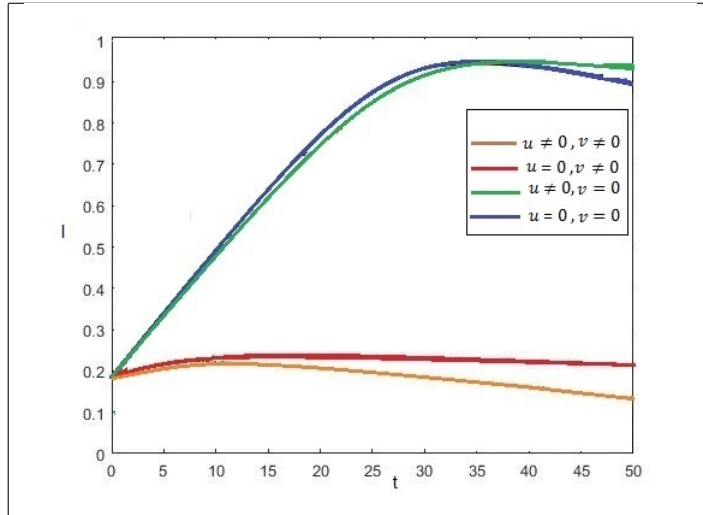


Figure 4: The behavior of I both with control and without control.

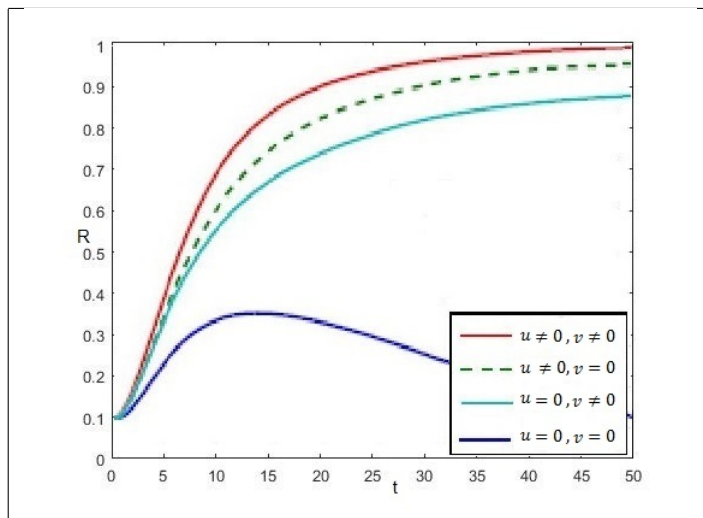


Figure 5: The behavior of R both with control and without control.

According to [Figure 4](#), the infected population will increase if it is not treated in order to control the incidence of the disease in society, and disease will turn into an epidemic, which will increase the vertical transmission in society. However, the infected population will decrease if the control and drug therapy increase, and with sustained drug therapy over time, vertical transmission will decrease and the disease will disappear.

According to [Figure 5](#), if we only use drug therapy to control the infected population and vaccination is at zero, the number of recovered population will increase in a certain period of time. If we only use the vaccination of the susceptible population to control the disease and drug therapy is at zero, with the increase of vaccination and the continuation of it at the social level, the number of recovered population will increase. If we simultaneously use both vaccination and drug therapy to control and prevent the incidence of the disease at the social level, the speed in the increase of recovered population increase will be very high compared to the previous two cases and this method of controlling infectious diseases at the social level will have good results.

6. Conclusions

In this paper, we study a fractional-order mathematical model in Caputo sense of order $\alpha \in (0, 1]$ for the transmission dynamics of infectious disease, under administration of vaccination and treatment. By the use of the fractional differential, we extended the classical *SEIR* mathematical modeling of infectious disease transmission to a system of fractional ordinary differential equations. For our fractional-order model, stability of equilibrium points is studied. Under certain conditions, an analysis of the local asymptotic stability at the disease-free equilibrium is given. In this work, under certain conditions and by construct suitable Lyapunov functionals it is proven that the infected steady-state is globally asymptotically stability. Then, we formulated a fractional optimal control problem and derived the fractional optimality condition for the control infectious disease by using Pontryagin's maximum principle. Finally, a numerical simulation of the optimal control problem are conducted to demonstrate our theoretical results. The simultaneous use of vaccination and drug therapy will be a highly effective strategy to control the disease in society. Hopefully, future research will explore the effects of two other controllers in addition to these two controllers of vaccination and drug therapy, such as quarantining infected people and masking everybody in the community.

Conflicts of Interest. The authors declare that they have no conflicts of interest regarding the publication of this article.

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Reza Akbari
Department of Mathematics,
Payame Noor University, (PNU),
Tehran, I. R. Iran
e-mail: r.akbari@pnu.ac.ir

Leader Navaei
Department of Statistics,
Payame Noor University, (PNU),
Tehran, I. R. Iran
e-mail: l.navaei@pnu.ac.ir