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Useful Results for Qualitative Analysis of the Generalized Hattaf Mixed Fractional Differential Equations with Application to Medicine

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Abstract: Most solutions of fractional differential equations (FDEs) that model real-world phenomena arising in various fields of science, industry and engineering are complex and cannot be solved analytically. This paper mainly aims to present some useful results for studying the qualitative properties of solutions of FDEs involving the new generalized Hattaf mixed (GHM) fractional derivative, which encompasses many types of fractional operators with both singular and non-singular kernels. Furthermore, the obtained results are applied to linear system arising from medicine.

Keywords: fractional calculus; Hattaf fractional derivative; fractional differential equations; comparaison principle; pharmacokinetics

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1. Introduction

Nowadays, fractional differential equations (FDEs) have become a powerful tool for modeling complex systems that exhibit non-local dynamics, memory effects, hereditary properties and anomalous behavior, which cannot be accurately described using classical ordinary differential equations (ODEs). For example, FDEs have been used in biology to model biological complexity, from subcellular processes to ecosystem dynamics. Their ability to capture memory, heterogeneity and anomalous transport makes them a significant contributor to the development of predictive biology, precision medicine and bioengineering.

In the literature, FDEs have been widely applied across many fields and they have been formulated by means of various fractional operators, such as the Caputo fractional derivative [1], the Caputo-Fabrizio (CF) fractional derivative [2], the Atangana-Baleanu (AB) fractional derivative [3], the weighted AB fractional derivative [4], the generalized Hattaf fractional (GHF) derivative [5], the Hattaf mixed fractional derivative [6], the Hadamard fractional derivative [7,8] and the Katugampola fractional derivative [9]. More recently, a new generalized Hattaf mixed (GHM) fractional derivative has been introduced in [10] to include all the above cited fractional derivatives [1–9] and other types like the new weighted fractional derivative with respect to another function [11], the generalized AB fractional derivative with generalized Mittag-Leffler function [12], the AB fractional derivative with respect to another function [13], the weighted CF fractional derivative with respect to another function [14], the power fractional derivative [15], as well as the modified fractional derivative [16].

The qualitative analysis of FDEs has been studied by several researchers based on various inequalities. For instance, Aguila-Camacho et al. [17] established a useful inequality for the Caputo fractional derivative of the quadratic Lyapunov function to prove the stability of numerous fractional systems. This useful inequality has been extended to investigate the stability of FDEs with AB fractional derivative [18], with Hadamard fractional derivative [19], with GHF derivative [20], as well as with generalized proportional Caputo fractional derivative [21]. Another idea given by Vargas-De-León [22] aims to extend the Volterra-type Lyapunov function to fractional-order epidemic systems via an

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inequality allowing to estimate the Caputo fractional derivative of this function. Similarly, the last inequality has been extended to the Caputo fractional derivative with respect to another function in [23], to the GHF derivative in [20], and to the AB fractional derivative in [18].

On the other hand, the stability analysis of fractional nonlinear systems involving the Caputo fractional derivative was studied by Delavari et al. [24] by means of Bihari and Bellman-Gronwall inequalities [25,26]. An extension of comparison principle to Hadamard fractional derivative was used by Wang et al. [27] to analyze the stability a class of nonlinear Hadamard type fractional differential system. A new version of fractional comparison principle has been introduced in [28] to discuss the qualitative properties of FDEs with the GHF derivative like the stability, the asymptotic stability and the Mittag-Leffler stability. Such new version extends the result presented in [29] with Caputo fractional derivative and the othor in [24] with Riemann-Liouville fractional derivative.

The contribution of this study is twofold: (i) to extend the aforementioned inequalities, and (ii) to establish significant and practical results for investigating the qualitative properties of FDEs involving the GHM fractional derivative, which generalizes numerous fractional operators with singular and non-singular kernels existing in the literature. To achieve these objectives, the remainder of this paper is organized as follows: Section 2 introduces key preliminary concepts and results required for the subsequent analysis. Section 3 is devoted to the main results of the study, including generalizations of several known inequalities and the extension of the comparison principle to the GHM fractional derivative. Finally, Section 4 presents an application of our main analytical results to a linear system in the field of medicine.

2. Preliminary Concepts and Results

This section recalls the concepts related to the new GMH fractional derivative and presents some preliminary results necessary for the present study.

Definition 2.1. *([10]) Let $(p,q) \in [0,1]^2$, $r, m > 0$, $Re(\mu) > 0$, $\sigma \in \mathbb{R}$, $\delta \in \mathbb{R}^*$ and $f \in \mathcal{H}^1(a,b)$. The GHM fractional derivative of the function $f(t)$ of order p in Caputo sense with the weight function $w(t)$ and respect to another function $\phi(t)$ is defined as follows*

$$ {}^{C}D^{p,q,r,m,\mu}_{a,\sigma,\delta,w,\phi} f(t) = \frac{H(p+q-1)}{(2-p-q)w(t)} \int_a^t (\phi(t)-\phi(\tau))^{\mu-1} E^{\sigma}_{r,\mu}[-\lambda^{\delta}_{p,q}(\phi(t)-\phi(\tau))^m](wf)'(\tau)d\tau, \quad (1) $$

where $w, \phi \in C^1(a,b)$, $w, \phi' > 0$ on $[a,b]$, $H(.)$ is a normalization function such that $H(0) = H(1) = 1$, $\lambda^{\delta}_{p,q} = \dfrac{\delta(p+q-1)}{2-p-q}$ and $E^{\sigma}_{r,\mu}(t) = \sum_{k=0}^{+\infty} \dfrac{(\sigma)_k t^k}{k!\Gamma(rk+\mu)}$ is the generalized Mittag-Leffler function of three parameters [30] with $(\sigma)_0 = 1$ and $(\sigma)_k = \sigma(\sigma+1)\cdots(\sigma+k-1)$ is the Pochhammer symbol.

It is important to note that the GHM fractional derivative given by Definition 2.1 includes numerous fractional derivatives with singular and non-singular kernels available in the literature. As examples, it becomes the new weighted fractional derivative with respect to another function [11] when $q = \delta = 1$, the GHF derivative [5] when $q = \delta = \mu = \sigma = 1$ and $\phi(t) = t$, the generalized AB fractional derivative with generalized Mittag-Leffler function [12] when $r = m = p$, $q = \delta = 1$, $w(t) = 1$ and $\phi(t) = t$, the weighted AB fractional derivative [4] when $r = m = p$, $q = \delta = \mu = \sigma = 1$ and $\phi(t) = t$, the AB fractional derivative with respect to another function [13] when $r = m = p$, $q = \delta = \mu = \sigma = 1$ and $w(t) = 1$, the AB fractional derivative [3] when $r = m = p$, $q = \delta = \mu = \sigma = 1$, $w(t) = 1$ and $\phi(t) = t$, the weighted CF fractional derivative with respect to another function [14] when $r = m = q = \delta = \mu = \sigma = 1$, the CF fractional derivative with respect to another function [14] when $r = m = q = \delta = \mu = \sigma = 1$ and $w(t) = 1$, the CF fractional derivative [2] when $r = m = q = \delta = \mu = \sigma = 1$, $w(t) = 1$ and $\phi(t) = t$, the Hattaf mixed fractional derivative [6] when $\mu = q$, $\sigma = 1$ and $\phi(t) = t$, the power fractional derivative [15] when $\mu = q = \sigma = 1$, $m = r$, $\delta = \ln(\bar{p})$ (with $\bar{p} > 0$) and $\phi(t) = t$, the fractional derivative introduced in [31] when $\mu = q$, $\sigma = \delta = 1$, $m = r = p$,

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$w(t)=1$ and $\phi(t)=t$, the modified fractional derivative [16] when $\mu=2-q$, $\sigma=\delta=1$, $m=r=p$, $w(t)=1$ and $\phi(t)=t$, the Caputo fractional derivative [1] when $\mu=q=1-p$, $w(t)=1$ and $\phi(t)=t$, the Hadamard fractional derivative [7,8] when $\mu=q=1-p$, $w(t)=1$ and $\phi(t)=\ln(t)$, as well as the Katugampola fractional derivative fractional derivative [9] when $\mu=q=1-p$, $w(t)=1$ and $\phi(t)=\frac{t^\rho}{\rho}$ with $\rho>0$.

Now, we recall the the fractional integral associated to the GHM fractional derivative.

Definition 2.2. *([10]) When $m=r$, the fractional integral associated to the GHM fractional derivative is defined as follows*

$$I^{p,q,r,\mu}_{a,\sigma,\delta,w,\phi}f(t)=\sum_{k=0}^{+\infty}\binom{\sigma}{k}\frac{\delta^k(p+q-1)^k}{(2-p-q)^{k-1}H(p+q-1)}\,{}^R\mathcal{I}^{kr-\mu+1}_{a,w,\phi}f(t), \tag{2}$$

where ${}^R\mathcal{I}^{\alpha}_{a,w,\phi}f(t)$ is the weighted Riemann-Liouville fractional integral of function $f(t)$ with respect to another $\phi(t)$ [32] given by

$${}^R\mathcal{I}^{\alpha}_{a,w,\phi}f(t)=\frac{1}{\Gamma(\alpha)w(t)}\int_a^t\phi'(\tau)\big(\phi(t)-\phi(\tau)\big)^{\alpha-1}(wf)(\tau)d\tau, \tag{3}$$

for $\alpha>0$ and ${}^R\mathcal{I}^{0}_{a,w,\phi}f(t)=f(t)$.

The generalized Hattaf fractional integral introduced in Definition 2.2 covers many forms of fractional integrals, including the generalized weighted fractional integral with respect to another function [11], the GHF integral [5], the fractional integral corresponding to the generalized AB fractional derivative with the generalized Mittag-Leffler function [12], the fractional integral corresponding to the generalized AB fractional derivative with the generalized Mittag-Leffler function [32], the weighted AB fractional integral [4], the AB fractional integral with respect to another function, the AB fractional integral [3], the weighted CF fractional integral with respect to another function [14], the CF fractional derivative [2], the fractional integral corresponding to the new mixed fractional derivative [6], the power fractional integral [15], the fractional integral introduced in [31], the modified fractional integral [16], the weighted Riemann-Liouville fractional integral with respect to another [32], the Hadamard fractional integral [33,34], the Katugampola fractional integral [35], the Riemann-Liouville fractional integral [36], the Riemann-Liouville fractional integral with respect to another function [36–38], as well as the tempered fractional integral [39,40].

Now, we recall the following fundamental result that extends the Newton-Leibniz formula presented in [36] for Caputo fractional derivative with singular kernel, in [6] for mixed fractional derivative, and in [41] for AB fractional derivative in Caputo sence.

Lemma 2.3. *Let $(p,q)\in[0,1]^2$, $r>0$, $Re(\mu)>0$, $\sigma\in\mathbb{R}$, $\delta\in\mathbb{R}^*$ and $f\in\mathcal{H}^1(a,b)$. Then*

$$I^{p,q,r,\mu}_{a,\sigma,\delta,w,\phi}\left({}^CD^{p,q,r,r,\mu}_{a,\sigma,\delta,w,\phi}f\right)(t)=f(t)-\frac{w(a)f(a)}{w(t)}.$$

Based on Theorem 2.6 of [10], we deduce the following result.

Lemma 2.4. *The weighted Laplace transform with respect to another function ϕ of the GHM fractional derivative is given by*

$$\mathcal{L}_{w,\phi}\{{}^CD^{p,q,r,r,\mu}_{a,\sigma,\delta,w,\phi}f(t)\}(s)=\frac{H(p+q-1)}{2-p-q}\sum_{k=0}^{+\infty}\frac{(\sigma)_k(-\lambda^{\delta}_{p,q})^k}{k!s^{km+\mu}}\left[s\mathcal{L}_{w,\phi}\{f(t)\}(s)-(wf)(a)\right],$$

where

$$\mathcal{L}_{w,\phi}\{f(t)\}(s)=\int_a^{+\infty}\phi'(t)e^{-s\left(\phi(t)-\phi(a)\right)}w(t)f(t)dt.$$

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3. Main Results

Let g be a continuous function and u be a continuously differentiable function. For any constant $\lambda \in \mathbb{R}$, we consider the following the function:

$$G(t) = \frac{1}{w(t)} \int_{\lambda}^{w(t)u(t)} g(x)dx. \tag{4}$$

Hence, we have

$$\begin{aligned} {}^{C}D^{p,q,r,m,\mu}_{a,\sigma,\delta,w,\phi}G(t) &= \frac{H(p+q-1)}{(2-p-q)w(t)} \int_a^t (\phi(t)-\phi(\tau))^{\mu-1} E^{\sigma}_{r,\mu}[-\lambda^{\delta}_{p,q}(\phi(t) \\ &\quad -\phi(\tau))^m] g(w(\tau)u(\tau))(wu)'(\tau)d\tau. \end{aligned}$$

We put,

$$g_1(t) = {}^{C}D^{p,q,r,m,\mu}_{a,\sigma,\delta,w,\phi}G(t) - g(w(t)u(t)){}^{C}D^{p,q,r,m,\mu}_{a,\sigma,\delta,w,\phi}u(t).$$

Thus,

$$g_1(t) = \frac{H(p+q-1)}{(2-p-q)w(t)} \int_a^t (\phi(t)-\phi(\tau))^{\mu-1} E^{\sigma}_{r,\mu}[-\lambda^{\delta}_{p,q}(\phi(t)-\phi(\tau))^m] v_1'(\tau)d\tau,$$

where

$$v_1(\tau) = g(w(t)u(t))(w(t)u(t) - w(\tau)u(\tau)) + \int_{w(t)u(t)}^{w(\tau)u(\tau)} g(x)dx.$$

Theorem 3.1. *For any constant $\lambda \in \mathbb{R}$, the GHM fractional derivative of the function $G(t)$ defined by (4) satisfies the following inequalities:*

(i) *When g is a increasing function and $\mu = \sigma = 1$ or $\mu = q = 1 - p$, we have*

$$ {}^{C}D^{p,q,r,m,\mu}_{a,\sigma,\delta,w,\phi}G(t) \le g(w(t)u(t)){}^{C}D^{p,q,r,m,\mu}_{a,\sigma,\delta,w,\phi}u(t). \tag{5}$$

(ii) *When g is a decreasing function and $\mu = \sigma = 1$ or $\mu = q = 1 - p$, we have*

$$ {}^{C}D^{p,q,r,m,\mu}_{a,\sigma,\delta,w,\phi}G(t) \ge g(w(t)u(t)){}^{C}D^{p,q,r,m,\mu}_{a,\sigma,\delta,w,\phi}u(t). \tag{6}$$

Proof. From integration by parts and using $\frac{d}{dt}E^{\sigma}_{r,\mu}(t) = \sigma E^{\sigma+1}_{r,r+\mu}(t)$, we get for $\mu = \sigma = 1$ that

$$\begin{aligned} g_1(t) &= \frac{H(p+q-1)}{(2-p-q)w(t)} E^1_{r,1}[-\lambda^{\delta}_{p,q}(\phi(t)-\phi(\tau))^m] v_1(\tau)|^{\tau=t}_{\tau=a} \\ &\quad - \frac{mH(p+q-1)\lambda^{\delta}_{p,q}}{(2-p-q)w(t)} \int_a^t v_1(\tau)\phi'(\tau)(\phi(t)-\phi(\tau))^{m-1} E^2_{r,r+1}[-\lambda^{\delta}_{p,q}(\phi(t)-\phi(\tau))^m]d\tau. \end{aligned}$$

Since $v_1(t) = 0$, we have

$$\begin{aligned} g_1(t) &= -\frac{H(p+q-1)v_1(a)}{(2-p-q)w(t)} E_r[-\lambda^{\delta}_{p,q}(\phi(t)-\phi(a))^m] \\ &\quad - \frac{mH(p+q-1)\lambda^{\delta}_{p,q}}{(2-p-q)w(t)} \int_a^t v_1(\tau)\phi'(\tau)(\phi(t)-\phi(\tau))^{m-1} E^2_{r,r+1}[-\lambda^{\delta}_{p,q}(\phi(t)-\phi(\tau))^m]d\tau. \end{aligned}$$

Define the following function:

$$\psi_{\lambda,g}(\tau) = g(\lambda)(\lambda-\tau) + \int_{\lambda}^{\tau} g(x)dx.$$

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Obviously, $\psi'_{\lambda,g}(\tau) = g(\tau) - g(\lambda)$. When g is an increasing function, we have $\psi_{\lambda,g}(\tau)$ is decreasing on the interval $(-\infty, \lambda]$ and increasing on $[\lambda, +\infty)$ with $\psi_{\lambda,g}(\lambda) = 0$. Then $\psi_{\lambda,g}(\tau)$ has the global minimum at $\tau = \lambda$. Hence,

$$\psi_{\lambda,g}(\tau) \geq 0, \text{ for all } (\lambda, \tau) \in \mathbb{R}^2.$$

As $v_1(\tau) = \psi_{w(t)u(t),g}(w(\tau)u(\tau))$, we obtain $v_1(\tau) \geq 0$ for all $\tau \in \mathbb{R}$. Similarly, we can easily prove that $v_1(\tau) \leq 0$ for all $\tau \in \mathbb{R}$ when g is decreasing function. This proves (i) when $\mu = \sigma = 1$.

For $\mu = q = 1 - p$, the expression of $g_1(t)$ becomes as follows

$$\begin{aligned} g_1(t) &= \frac{1}{\Gamma(1-p)w(t)} \int_a^t (\phi(t) - \phi(\tau))^{-p} v_1'(\tau) d\tau \\ &= \frac{1}{\Gamma(1-p)w(t)} (\phi(t) - \phi(\tau))^{-p} v_1(\tau)|_{\tau=a}^{\tau=t} \\ &\quad - \frac{p}{\Gamma(1-p)w(t)} \int_a^t v_1(\tau)\phi'(\tau)(\phi(t) - \phi(\tau))^{-p-1} d\tau. \end{aligned}$$

Since $v_1'(t) = 0$, we have $\lim_{\tau \mathbb{R}ightarrow t} (\phi(t) - \phi(\tau))^{-p} v_1(\tau) = 0$. Hence,

$$g_1(t) = -\frac{v_1(a)(\phi(t) - \phi(a))^{-p}}{\Gamma(1-p)w(t)} - \frac{p}{\Gamma(1-p)w(t)} \int_a^t v_1(\tau)\phi'(\tau)(\phi(t) - \phi(\tau))^{-p-1} d\tau.$$

This proves (ii) for $\mu = q = 1 - p$. ∎

Corollary 3.2. *Let $u(t) \in \mathbb{R}$ be a continuously differentiable function. Then, at any time $t \geq a$, for $\mu = \sigma = 1$ or $\mu = q = 1 - p$, we have*

$$^C D^{p,q,r,m,\mu}_{a,\sigma,\delta,w,\phi} w(t) u^2(t) \leq 2w(t)u(t)\, ^C D^{p,q,r,m,\mu}_{a,\sigma,\delta,w,\phi} u(t). \tag{7}$$

Proof. By applying Theorem 3.1 (i) to the function $g(x) = 2x$, we have

$$\begin{aligned} ^C D^{p,q,r,m,\mu}_{a,\sigma,\delta,w,\phi} w(t) u^2(t) &= {}^C D^{p,q,r,m,\mu}_{a,\sigma,\delta,w,\phi} \left(\frac{1}{w(t)} \int_\lambda^{u(t)w(t)} 2x dx \right) \\ &\leq 2w(t)u(t)\, ^C D^{p,q,r,m,\mu}_{a,\sigma,\delta,w,\phi} u(t). \end{aligned}$$

This completes the proof of Corollary 3.2. ∎

Remark 3.3. *Corollary 3.2 generalizes and extends various results existing in the literature. For instance,*

- *When $\mu = \sigma = q = \delta = 1$, $w(t) = 1$ and $\phi(t) = t$, we get Corollary 1 of [20] for GHF derivative.*
- *When $\mu = \sigma = q = \delta = 1$, $r = m = p$, $w(t) = 1$ and $\phi(t) = t$, we obtain Lemma 3.1 of [18] for AB fractional derivative.*
- *When $\mu = q = 1 - p$, $w(t) = 1$ and $\phi(t) = t$, we get Lemma 1 of [17] for Caputo fractional derivative.*
- *When $\mu = q = 1 - p$, $w(t) = 1$ and $\phi(t) = \ln(t)$, we get Remark 3 of [19] for Caputo fractional derivative.*
- *When $\mu = q = 1 - p$, $w(t) = e^{-\frac{\rho-1}{\rho}t}$ and $\phi(t) = \frac{t}{\rho}$ with $\rho \in (0, 1]$, we obtain Lemma 1 of [21] for generalized proportional Caputo fractional derivative [42,43].*

Corollary 3.4. *Let $u(t) \in \mathbb{R}^+$ be a continuously differentiable function and $u^* > 0$. Then, at any time $t \geq a$, for $\mu = \sigma = 1$ or $\mu = q = 1 - p$, we have*

$$^C D^{p,q,r,m,\mu}_{a,\sigma,\delta,w,\phi} [u(t) - \frac{u^*}{w(t)} - \frac{u^*}{w(t)} \ln(\frac{u(t)w(t)}{u^*})] \leq \left(1 - \frac{u^*}{w(t)u(t)}\right) {}^C D^{p,q,r,m,\mu}_{a,\sigma,\delta,w,\phi} u(t). \tag{8}$$

Proof. For $g(x) = \frac{1}{x}$, we have $G(t) = \frac{1}{w(t)} \ln(\frac{u(t)w(t)}{u^*})$.
Since $x \mapsto \frac{1}{x}$ is a decreasing function on $(0, +\infty)$, it follows from Theorem 3.1 (ii) that

$$^C D^{p,q,r,m,\mu}_{a,\sigma,\delta,w,\phi} G(t) \geq g(w(t)u(t)) ^C D^{p,q,r,m,\mu}_{a,\sigma,\delta,w,\phi} u(t),$$

which implies that

$$^C D^{p,q,r,m,\mu}_{a,\sigma,\delta,w,\phi} [\frac{1}{w(t)} \ln(\frac{u(t)w(t)}{u^*})] \geq \frac{1}{w(t)u(t)} {}^C D^{p,q,r,m,\mu}_{a,\sigma,\delta,w,\phi} u(t).$$

Then

$$^C D^{p,q,r,m,\mu}_{a,\sigma,\delta,w,\phi} [u(t) - \frac{u^*}{w(t)} \ln(\frac{u(t)w(t)}{u^*})] \leq \left(1 - \frac{u^*}{w(t)u(t)}\right) {}^C D^{p,q,r,m,\mu}_{a,\sigma,\delta,w,\phi} u(t).$$

Since $^C D^{p,q,r,m,\mu}_{a,\sigma,\delta,w,\phi} (\frac{u^*}{w(t)}) = 0$, we have

$$^C D^{p,q,r,m,\mu}_{a,\sigma,\delta,w,\phi} [u(t) - \frac{u^*}{w(t)} - \frac{u^*}{w(t)} \ln(\frac{u(t)w(t)}{u^*})] \leq \left(1 - \frac{u^*}{w(t)u(t)}\right) {}^C D^{p,q,r,m,\mu}_{a,\sigma,\delta,w,\phi} u(t).$$

This completes the proof of Corollary 3.4. ■

Remark 3.5. *Corollary 3.4 generalizes and extends many inequalities used to establish the global stability of FDEs. For example,*

- *When $\mu = q = 1 - p$ and $w(t) = 1$, we obtain the recent result presented in Theorem 5 of [23].*
- *When $\mu = \sigma = q = \delta = 1$, $w(t) = 1$ and $\phi(t) = t$, we get Corollary 2 of [20] for GHF derivative.*
- *When $\mu = q = 1 - p$, $w(t) = 1$ and $\phi(t) = t$, we get Lemma 3.1. of [22] for Caputo fractional derivative.*
- *When $\mu = \sigma = q = \delta = 1$, $r = m = p$, $w(t) = 1$ and $\phi(t) = t$, we obtain Lemma 3.2 of [18] for AB fractional derivative.*

Theorem 3.6. *Let $u(t) \in \mathbb{R}^n$ be a continuously differentiable function and $P \in \mathbb{R}^{n\times n}$ be a symmetric positive definite matrix. Then, at any time $t \geq a$, for $\mu = \sigma = 1$ or $\mu = q = 1 - p$, we have*

$$^C D^{p,q,r,m,\mu}_{a,\sigma,\delta,w,\phi} (w(t)u(t)^T P u(t)) \leq 2w(t)u(t)^T P {}^C D^{p,q,r,m,\mu}_{a,\sigma,\delta,w,\phi} u(t). \quad (9)$$

Proof. Consider the following function

$$g_2(t) = {}^C D^{p,q,r,m,\mu}_{a,\sigma,\delta,w,\phi} (w(t)u(t)^T P u(t)) - 2w(t)u(t)^T P {}^C D^{p,q,r,m,\mu}_{a,\sigma,\delta,w,\phi} u(t). \quad (10)$$

Then

$$\begin{aligned} g_2(t) &= \frac{H(p+q-1)}{(2-p-q)w(t)} \int_a^t (\phi(t) - \phi(\tau))^{\mu-1} E^{\sigma}_{r,\mu}[-\lambda^{\delta}_{p,q} (\phi(t) - \phi(\tau))^m] (2v_2(\tau)^T P \dot{v}_2(\tau)) d\tau \\ &= \frac{N(\alpha)}{1-\alpha} \int_{t_0}^t E_\beta[-\mu_\alpha (t-\tau)^\gamma] (y(\tau)^T P \dot{y}(\tau))' d\tau, \end{aligned}$$

where $v_2(\tau) = w(\tau)u(\tau) - w(t)u(t)$. Hence,

$$g_2(t) = \frac{H(p+q-1)}{(2-p-q)w(t)} \int_a^t (\phi(t) - \phi(\tau))^{\mu-1} E^{\sigma}_{r,\mu}[-\lambda^{\delta}_{p,q} (\phi(t) - \phi(\tau))^m] (v_2(\tau)^T P \dot{v}_2(\tau))' d\tau,$$

Integrating by parts, we get for $\mu = \sigma = 1$ that

$$g_2(t) = \frac{H(p+q-1)}{(2-p-q)w(t)}\Big\{E^1_{r,1}[-\lambda^\delta_{p,q}(\phi(t)-\phi(\tau))^m]v_2(\tau)^T P v_2(\tau)|_{\tau=a}^{\tau=t} - m\lambda^\delta_{p,q}\int_a^t \phi'(\tau)(\phi(t)-\phi(\tau))^{m-1}E^2_{r,r+1}[-\lambda^\delta_{p,q}(\phi(t)-\phi(\tau))^m]v_2(\tau)^T P v_2(\tau)d\tau\Big\}.$$

Since $\lim_{\tau\to t} E^1_{r,1}[-\lambda^\delta_{p,q}(\phi(t)-\phi(\tau))^m]v_2(\tau)^T P v_2(\tau) = v_2(t)^T P v_2(t) = 0$, we have

$$g_2(t) = -\frac{H(p+q-1)}{(2-p-q)w(t)}\Big\{E^1_{r,1}[-\lambda^\delta_{p,q}(\phi(t)-\phi(\tau))^m]v_2(a)^T P v_2(a) + m\lambda^\delta_{p,q}\int_a^t \phi'(\tau)(\phi(t)-\phi(\tau))^{m-1}E^2_{r,r+1}[-\lambda^\delta_{p,q}(\phi(t)-\phi(\tau))^m]v_2(\tau)^T P v_2(\tau)d\tau\Big\}.$$

On the other hand, the expression of $g_2(t)$ for $\mu = q = 1-p$ becomes as follows

$$g_2(t) = \frac{1}{\Gamma(1-p)w(t)}\Big\{(\phi(t)-\phi(\tau))^{-p}v_2(\tau)^T P v_2(\tau)|_{\tau=a}^{\tau=t} - p\int_a^t \phi'(\tau)(\phi(t)-\phi(\tau))^{-p-1}v_2(\tau)^T P v_2(\tau)d\tau\Big\}.$$

By Hospital's rule, we have

$$\lim_{\tau\to t}\frac{v_2(\tau)^T P v_2(\tau)}{(\phi(t)-\phi(\tau))^p} = \lim_{\tau\to t}\frac{2v_2(\tau)^T P\dot{v}_2(\tau)}{-p\phi'(\tau)(\phi(t)-\phi(\tau))^{p-1}} = 0.$$

Hence,

$$g_2(t) = \frac{-(\phi(t)-\phi(a))^{-p}}{\Gamma(1-p)w(t)}v_2(a)^T P v_2(a) - \frac{p}{\Gamma(1-p)w(t)}\int_a^t \phi'(\tau)(\phi(t)-\phi(\tau))^{-p-1}v_2(\tau)^T P v_2(\tau)d\tau.$$

Therefore, $g_2(t) \le 0$ for all $t \ge a$ when $\mu = \sigma = 1$ or $\mu = q = 1-p$, which implies that

$${}^C D^{p,q,r,m,\mu}_{a,\sigma,\delta,w,\phi}(w(t)u(t)^T P u(t)) \le 2w(t)u(t)^T P\, {}^C D^{p,q,r,m,\mu}_{a,\sigma,\delta,w,\phi}u(t).$$

The proof is completed. ■

Remark 3.7. *Theorem 3.6 extends and generalizes many recent results available to previous studies. More precisely, Theorem 3.6 coincides with*

(i) *Lemma 2.5 of [44] when $\mu = q = 1-p$, $w(t) = 1$ and $\phi(t) = \frac{t^\rho}{\rho}$ with $\rho > 0$;*

(ii) *Corollary 1 of [23] when $\mu = q = 1-p$, $w(t) = 1$ and $P = I_n$;*

(iii) *Lemma 1 of [45] when $\mu = \sigma = q = \delta = 1$, $w(t) = 1$ and $\phi(t) = t$, which covers the results presented in [18,20,46].*

Theorem 3.8. *(Fractional comparison principle). Let $u(t)$ and $v(t)$ two functions defined on the interval $[t_0, +\infty)$ with ${}^C D^{p,q,r,m,\mu}_{a,\sigma,\delta,w,\phi}u(t) \ge {}^C D^{p,q,r,m,\mu}_{a,\sigma,\delta,w,\phi}v(t)$ and $u(t_0) \ge v(t_0)$. Then $u(t) \ge v(t)$, for all $t \ge t_0$.*

Proof. Since ${}^C D^{p,q,r,m,\mu}_{a,\sigma,\delta,w,\phi}u(t) \ge {}^C D^{p,q,r,m,\mu}_{a,\sigma,\delta,w,\phi}v(t)$, it follows from Lemma 2.3 that

$$u(t) - \frac{u(t_0)w(t_0)}{w(t)} \ge v(t) - \frac{v(t_0)w(t_0)}{w(t)},$$

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which leads to

$$u(t) \geq v(t) + \frac{w(t_0)\big(u(t_0) - v(t_0)\big)}{w(t)}.$$

As $u(t_0) \geq v(t_0)$, we have $u(t) \geq v(t)$, for all $t \geq t_0$. ∎

Remark 3.9. *Theorem 3.8 extends three results, the first in Lemma 6.1 of [29] with Caputo fractional derivative, the second in Theorem 2.4 of [24] with Riemann-Liouville fractional derivative, and the third in Lemma 1 of [28] with GHF derivative.*

As in [47], the weighted convolution of functions f and g is defined by

$$(f *_{w,\phi} g)(t) \quad = \quad \frac{1}{w(t)} \int_a^t w\big(\phi(t) + \phi(a) - \phi(\tau)\big) f\big(\phi^{-1}(\phi(t) + \phi(a) - \phi(\tau))\big) w(\tau) g(\tau) \phi'(\tau) d\tau.$$

Obviously, we have

$$\mathcal{L}_{w,\phi}\{f *_{w,\phi} g\} = \mathcal{L}_{w,\phi}\{f\}\mathcal{L}_{w,\phi}\{g\}.$$

Theorem 3.10. *Let α be a constant, $y(t)$ and $u(t)$ be two functions such that*

$$^{C}D^{p,q,r,r,\mu}_{a,\sigma,\delta,w,\phi} y(t) = \alpha y(t) + u(t). \tag{11}$$

(i) *If $\mu = \sigma = 1$, then*

$$\begin{aligned} y(t) \quad &= \quad \frac{H(p+q-1)w(a)y(a)}{a_{p,q}w(t)} E_r\Big[\frac{\delta\alpha(p+q-1)}{a_{p,q}}\big(\phi(t) - \phi(a)\big)^r\Big] + \frac{2-p-q}{a_{p,q}} u(t) \\ &+ \frac{\delta(p+q-1)H(p+q-1)}{a^2_{p,q}} \left(\frac{E_{r,r}\big[\frac{\delta\alpha(p+q-1)}{a_{p,q}}\big(\phi(t) - \phi(a)\big)^r\big]}{w(t)\big(\phi(t) - \phi(a)\big)^{1-r}} *_{w,\phi} u(t) \right), \end{aligned}$$

where $a_{p,q} = H(p+q-1) - \alpha(2-p-q) \neq 0$ and $\alpha \neq 0$.

(ii) *If $\mu = q = 1 - p$, then*

$$y(t) \quad = \quad \frac{w(a)y(a)}{w(t)} E_p\big[\alpha\big(\phi(t) - \phi(a)\big)^p\big] + \frac{E_{p,p}\big[\alpha\big(\phi(t) - \phi(a)\big)^p\big]}{w(t)\big(\phi(t) - \phi(a)\big)^{1-p}} *_{w,\phi} u(t).$$

Proof. By applying the weighed Laplace transform $\mathcal{L}_{w,\phi}$ to both sides of (11) and using Lemma (2.4), we get for $\mu = \sigma = 1$ that

$$\begin{aligned} \mathcal{L}_{w,\phi}\{y(t)\}(s) \quad &= \quad \frac{H(p+q-1)w(a)y(a)s^{r-1}}{[H(p+q-1) - \alpha(2-p-q)]s^r - \delta(p+q-1)\alpha} \\ &+ \frac{[(2-p-q)s^r + \delta(p+q-1)]\mathcal{L}_{w,\phi}\{u(t)\}(s)}{[H(p+q-1) - \alpha(2-p-q)]s^r - \delta(p+q-1)\alpha}. \end{aligned}$$

Since $a_{p,q} = H(p+q-1) - \alpha(2-p-q) \neq 0$, we have

$$\begin{aligned}\mathcal{L}_{w,\phi}\{y(t)\}(s) &= \frac{H(p+q-1)w(a)y(a)}{a_{p,q}}\frac{s^{r-1}}{s^r - \frac{\delta\alpha(p+q-1)}{a_{p,q}}} + \frac{2-p-q}{a_{p,q}}\mathcal{L}_{w,\phi}\{u(t)\}(s) \\ &+ \frac{\delta(p+q-1)H(p+q-1)}{a_{p,q}^2}\frac{1}{s^r - \frac{\delta\alpha(p+q-1)}{a_{p,q}}}, \\ &= \frac{H(p+q-1)w(a)y(a)}{a_{p,q}}\mathcal{L}_{w,\phi}\{w^{-1}(t)E_r[\frac{\delta\alpha(p+q-1)}{a_{p,q}}(\phi(t)-\phi(a))^r]\}(s) \\ &+ \frac{2-p-q}{a_{p,q}}\mathcal{L}_{w,\phi}\{u(t)\}(s) \\ &+ \frac{\delta(p+q-1)H(p+q-1)}{a_{p,q}^2}\mathcal{L}_{w,\phi}\{\frac{E_{r,r}[\frac{\delta\alpha(p+q-1)}{a_{p,q}}(\phi(t)-\phi(a))^r]}{w(t)(\phi(t)-\phi(a))^{1-r}}\}\mathcal{L}_{w,\phi}\{u(t)\}.\end{aligned}$$

Hence,

$$\begin{aligned}y(t) &= \frac{H(p+q-1)w(a)y(a)}{a_{p,q}w(t)}E_r[\frac{\delta\alpha(p+q-1)}{a_{p,q}}(\phi(t)-\phi(a))^r] + \frac{2-p-q}{a_{p,q}}u(t) \\ &+ \frac{\delta(p+q-1)H(p+q-1)}{a_{p,q}^2}\left(\frac{E_{r,r}[\frac{\delta\alpha(p+q-1)}{a_{p,q}}(\phi(t)-\phi(a))^r]}{w(t)(\phi(t)-\phi(a))^{1-r}} *_{w,\phi} u(t)\right),\end{aligned}$$

This proves (i). For $\mu = q = 1-p$, we have

$$\begin{aligned}\mathcal{L}_{w,\phi}\{y(t)\}(s) &= w(a)y(a)\frac{s^{p-1}}{s^p-\alpha} + \frac{1}{s^p-\alpha}\mathcal{L}_{w,\phi}\{u(t)\}(s), \\ &= w(a)y(a)\mathcal{L}_{w,\phi}\{w^{-1}(t)E_p[\alpha(\phi(t)-\phi(a))^p]\}(s) \\ &\quad + \mathcal{L}_{w,\phi}\{w^{-1}(t)(\phi(t)-\phi(a))^{p-1}E_{p,p}[\alpha(\phi(t)-\phi(a))^p]\}\mathcal{L}_{w,\phi}\{u(t)\},\end{aligned}$$

which implies that

$$y(t) = \frac{w(a)y(a)}{w(t)}E_p[\alpha(\phi(t)-\phi(a))^p] + \frac{E_{p,p}[\alpha(\phi(t)-\phi(a))^p]}{w(t)(\phi(t)-\phi(a))^{1-p}} *_{w,\phi} u(t).$$

This proves (ii). ■

Corollary 3.11. *Let $\alpha > 0$ and $f(t)$ be a function such that*

$$^{C}D^{p,q,r,r,\mu}_{0,\sigma,\delta,w,\phi}f(t) \leq -\alpha f(t). \tag{12}$$

(i) *If $\mu = \sigma = 1$, then*

$$f(t) \leq f(0)E_r\left(\frac{-\delta\alpha(p+q-1)(\phi(t)-\phi(0))^r}{H(p+q-1)+\alpha(2-p-q)}\right).$$

(ii) *If $\mu = q = 1-p$, then*

$$f(t) \leq f(0)E_p\left(\alpha(\phi(t)-\phi(0))^p\right).$$

Proof. It follows from (12) that there exists a nonnegative function $u(t)$ such that

$$^{C}D^{p,q,r,r,\mu}_{0,\sigma,\delta,w,\phi}f(t) = -\alpha f(t) - u(t).$$

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According to Theorem 3.10, we have for $\mu = \sigma = 1$ that

$$\begin{aligned} f(t) &= \frac{H(p+q-1)w(0)f(0)}{w(t)(H(p+q-1)+\alpha(2-p-q))} E_r\left(\frac{-\delta\alpha(p+q-1)(\phi(t)-\phi(0))^r}{H(p+q-1)+\alpha(2-p-q)}\right) \\ &\quad - \frac{2-p-q}{H(p+q-1)+\alpha(2-p-q)} u(t) \\ &\quad - \frac{\delta(p+q-1)H(p+q-1)}{(H(p+q-1)+\alpha(2-p-q))^2}\left(\frac{E_{r,r}[-\frac{\delta\alpha(p+q-1)}{H(p+q-1)+\alpha(2-p-q)}(\phi(t)-\phi(0))^r]}{w(t)(\phi(t)-\phi(0))^{1-r}} *_{w,\phi} u(t)\right). \end{aligned}$$

Since $u(t) \geq 0$ and $w(0) \leq w(t)$ for $t \geq 0$, we get

$$f(t) \leq f(0)E_r\left(\frac{-\delta\alpha(p+q-1)(\phi(t)-\phi(0))^r}{H(p+q-1)+\alpha(2-p-q)}\right).$$

Similarly, we obtain for $\mu = q = 1-p$ that

$$f(t) = \frac{w(0)f(0)}{w(t)} E_p\left(\alpha(\phi(t)-\phi(0))^p\right) - \frac{E_{p,p}[\alpha(\phi(t)-\phi(0))^p]}{w(t)(\phi(t)-\phi(a))^{1-p}} *_{w,\phi} u(t).$$

Hence,

$$f(t) \leq f(0)E_p\left(\alpha(\phi(t)-\phi(0))^p\right).$$

■

Remark 3.12. *Corollary 3.11 includes the result given in [45], it suffices to take $q = \delta = 1$ and $\phi(t) = t$ in (i).*

Corollary 3.13. *Let $\alpha \in \mathbb{R}^+$, $f(t)$ and $u(t)$ be two nonnegative functions such that*

$$^C D^{p,q,r,r,\mu}_{0,\sigma,\delta,w,\phi} f(t) \leq \alpha f(t) + u(t). \tag{13}$$

(i) *If $\mu = \sigma = 1$, then*

$$\begin{aligned} f(t) &\leq \frac{H(p+q-1)w(a)f(a)}{a_{p,q}w(t)} E_r[\frac{\delta\alpha(p+q-1)}{a_{p,q}}(\phi(t)-\phi(a))^r] + \frac{2-p-q}{a_{p,q}} u(t) \\ &\quad + \frac{\delta(p+q-1)H(p+q-1)}{w(t)a_{p,q}^2}\Gamma(r)E_{r,r}[\frac{\delta\alpha(p+q-1)}{a_{p,q}}(\phi(t)-\phi(\tau))^r]^R\mathcal{I}^r_{a,w,\phi}u(t). \end{aligned}$$

(ii) *If $\mu = q = 1-p$, then*

$$f(t) \leq \frac{w(a)f(a)}{w(t)} E_p[\alpha(\phi(t)-\phi(a))^p] + \Gamma(p)E_{p,p}[\alpha(\phi(t)-\phi(a))^p]^R\mathcal{I}^p_{a,w,\phi}u(t).$$

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Proof. Let $\widetilde{u}(t) = {}^{C}D^{p,q,r,r,\mu}_{0,\sigma,\delta,w,\phi} f(t) - \alpha f(t)$. By applying Theorem 3.10, we have for $\mu = \sigma = 1$ that

$$\begin{aligned} f(t) &= \frac{H(p+q-1)w(a)f(a)}{a_{p,q}w(t)} E_r[\frac{\delta\alpha(p+q-1)}{a_{p,q}}(\phi(t)-\phi(a))^r] + \frac{2-p-q}{a_{p,q}}\widetilde{u}(t) \\ &+ \frac{\delta(p+q-1)H(p+q-1)}{a^2_{p,q}}\left(\frac{E_{r,r}[\frac{\delta\alpha(p+q-1)}{a_{p,q}}(\phi(t)-\phi(a))^r]}{w(t)(\phi(t)-\phi(a))^{1-r}} *_{w,\phi} \widetilde{u}(t)\right), \\ &= \frac{H(p+q-1)w(a)f(a)}{a_{p,q}w(t)} E_r[\frac{\delta\alpha(p+q-1)}{a_{p,q}}(\phi(t)-\phi(a))^r] + \frac{2-p-q}{a_{p,q}}\widetilde{u}(t) \\ &+ \frac{\delta(p+q-1)H(p+q-1)}{w(t)a^2_{p,q}} \int_a^t \frac{E_{r,r}[\frac{\delta\alpha(p+q-1)}{a_{p,q}}(\phi(t)-\phi(\tau))^r]}{(\phi(t)-\phi(\tau))^{1-r}} w(\tau)\widetilde{u}(\tau)\phi'(\tau)d\tau. \end{aligned}$$

Since $\widetilde{u}(t) \leq u(t)$, we have

$$\begin{aligned} f(t) &\leq \frac{H(p+q-1)w(a)f(a)}{a_{p,q}w(t)} E_r[\frac{\delta\alpha(p+q-1)}{a_{p,q}}(\phi(t)-\phi(a))^r] + \frac{2-p-q}{a_{p,q}}u(t) \\ &+ \frac{\delta(p+q-1)H(p+q-1)}{w(t)a^2_{p,q}} \int_a^t \frac{E_{r,r}[\frac{\delta\alpha(p+q-1)}{a_{p,q}}(\phi(t)-\phi(\tau))^r]}{(\phi(t)-\phi(\tau))^{1-r}} w(\tau)u(\tau)\phi'(\tau)d\tau, \\ &\leq \frac{H(p+q-1)w(a)f(a)}{a_{p,q}w(t)} E_r[\frac{\delta\alpha(p+q-1)}{a_{p,q}}(\phi(t)-\phi(a))^r] + \frac{2-p-q}{a_{p,q}}u(t) \\ &+ \frac{\delta(p+q-1)H(p+q-1)}{w(t)a^2_{p,q}}\Gamma(r)E_{r,r}[\frac{\delta\alpha(p+q-1)}{a_{p,q}}(\phi(t)-\phi(\tau))^r]\, {}^{R}\mathcal{I}^r_{a,w,\phi}u(t). \end{aligned}$$

By similar way, we get for $\mu = q = 1-p$ that

$$\begin{aligned} f(t) &= \frac{w(a)f(a)}{w(t)} E_p[\alpha(\phi(t)-\phi(a))^p] + \frac{E_{p,p}[\alpha(\phi(t)-\phi(a))^p]}{w(t)(\phi(t)-\phi(a))^{1-p}} *_{w,\phi} \widetilde{u}(t), \\ &= \frac{w(a)f(a)}{w(t)} E_p[\alpha(\phi(t)-\phi(a))^p] + \frac{1}{w(t)}\int_a^t \frac{E_{p,p}[\alpha(\phi(t)-\phi(\tau))^p]}{(\phi(t)-\phi(\tau))^{1-p}} w(\tau)\widetilde{u}(\tau)\phi'(\tau)d\tau, \\ &\leq \frac{w(a)f(a)}{w(t)} E_p[\alpha(\phi(t)-\phi(a))^p] + \Gamma(p)E_{p,p}[\alpha(\phi(t)-\phi(a))^p]\, {}^{R}\mathcal{I}^p_{a,w,\phi}u(t). \end{aligned}$$

This completes the proof. ■

Remark 3.14. *Corollary 3.13 covers the ϕ-Caputo Bellman-Gronwall inequality presented in Theorem 3 of [23], it suffices to take $w(t) = 1$ in (ii).*

4. Application

This section presents an application of the main obtained results to investigate a problem in pharmacokinetics, which is a branch of medicine that studies the absorption, distribution, metabolism and elimination of drugs in a living body.

To describe the dynamics of a drug concentration in a living body, we propose the following mathematical model with linear FDEs involving the GHM fractional derivative:

$$\begin{cases} {}^{C}D^{p,q,r,r,\mu}_{0,\sigma,\delta,w,\phi} y(t) = -dy(t), \\ y(0) = y_0, \end{cases} \tag{14}$$

where $y(t)$ represents the drug concentration in the body at time t, d is a positive constant that can be experimentally determined for each drug, as well as y_0 denotes the initial drug dose administered.

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By applying Theorem 3.10 for the case $\mu = q = 1 - p$, the solution of (14) is given by

$$y(t) = \frac{w(0)y_0}{w(t)} E_p\Big(-d\big(\phi(t) - \phi(0)\big)^p \Big). \tag{15}$$

In this situation, the pharmacokinetics model presented in 2022 by Awadalla et al. [48] for predicting drug concentration levels in human blood over time is a special case of (14). Furthermore, the solution of (14) given by (15) is reduced to that presented in [48] by choosing $w(t) = 1$.

For the situation $\mu = \sigma = 1$, the application of Theorem 3.10 gives that the solution of (14) is as follows:

$$y(t) = \frac{H(p+q-1)w(0)y_0}{[H(p+q-1) + d(2-p-q)]w(t)} E_r\Big(\frac{-d\delta(p+q-1)}{H(p+q-1) + d(2-p-q)} \big(\phi(t) - \phi(0)\big)^r \Big). \tag{16}$$

Let $d = 0.5459$, $w(t) = 1$, $\phi(t) = t + 1$ and $H(p) = 1$. Figures 1 and 2 present the graphs of solutions of the pharmacokinetics model (14) for different values of order p.

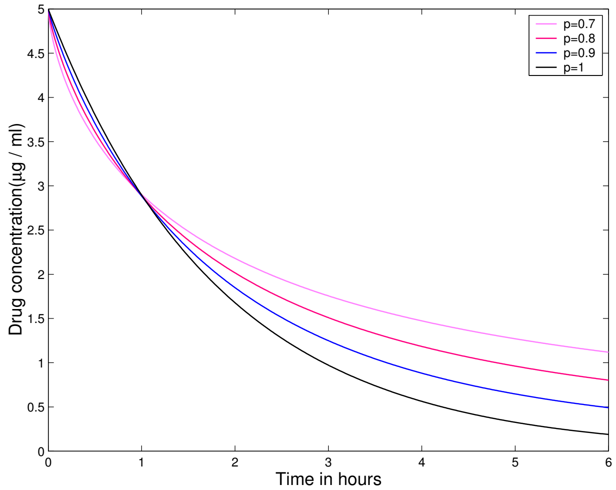

Figure 1. The graph of (15) for different values of order p.

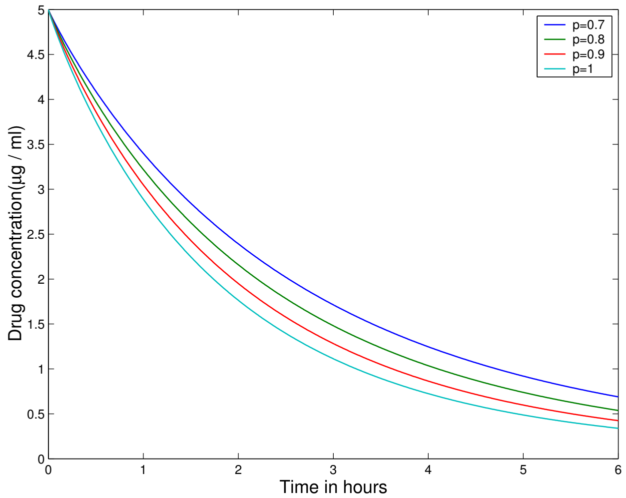

Figure 2. The graph of (16) for different values of p with $q = \delta = 1$ and $r = 0.8$.

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