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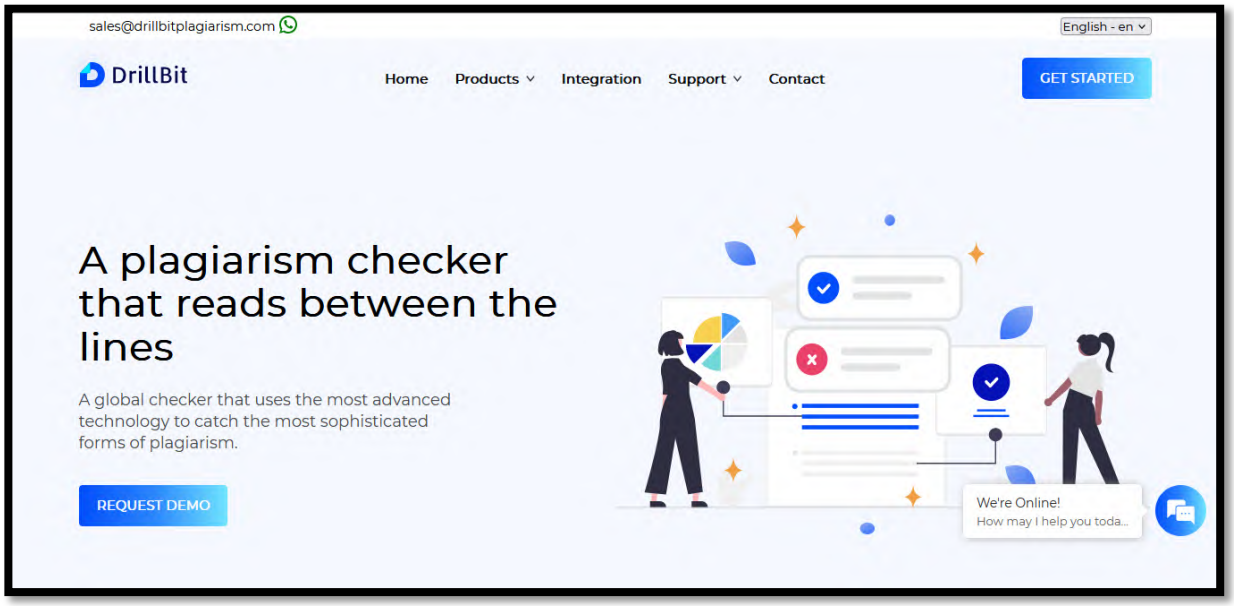

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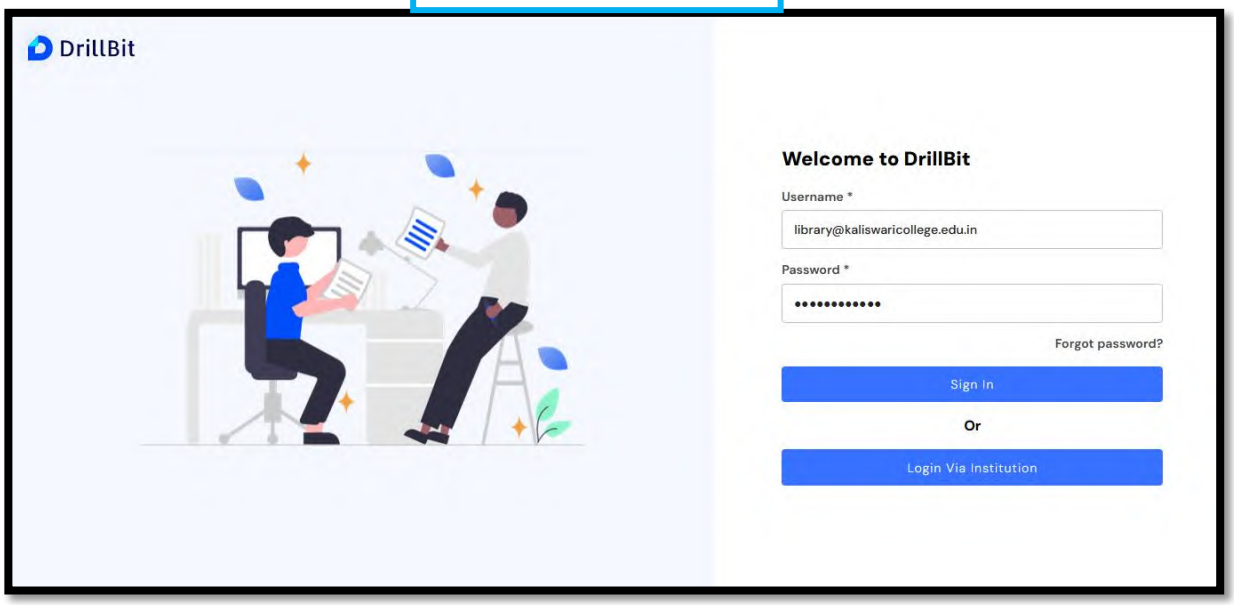

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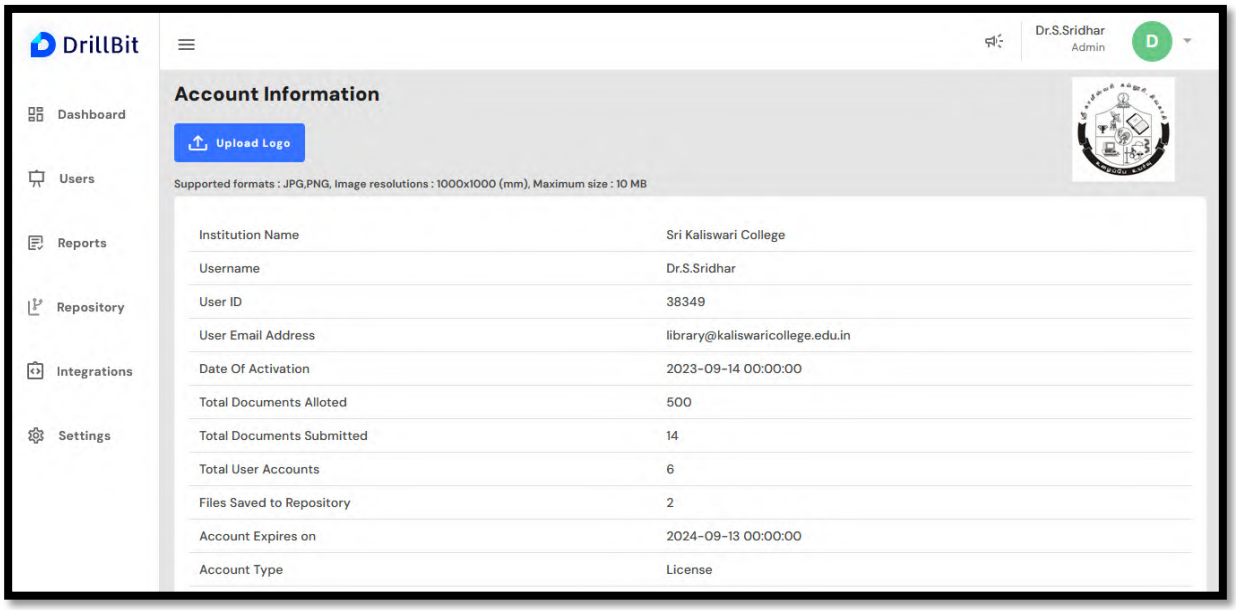

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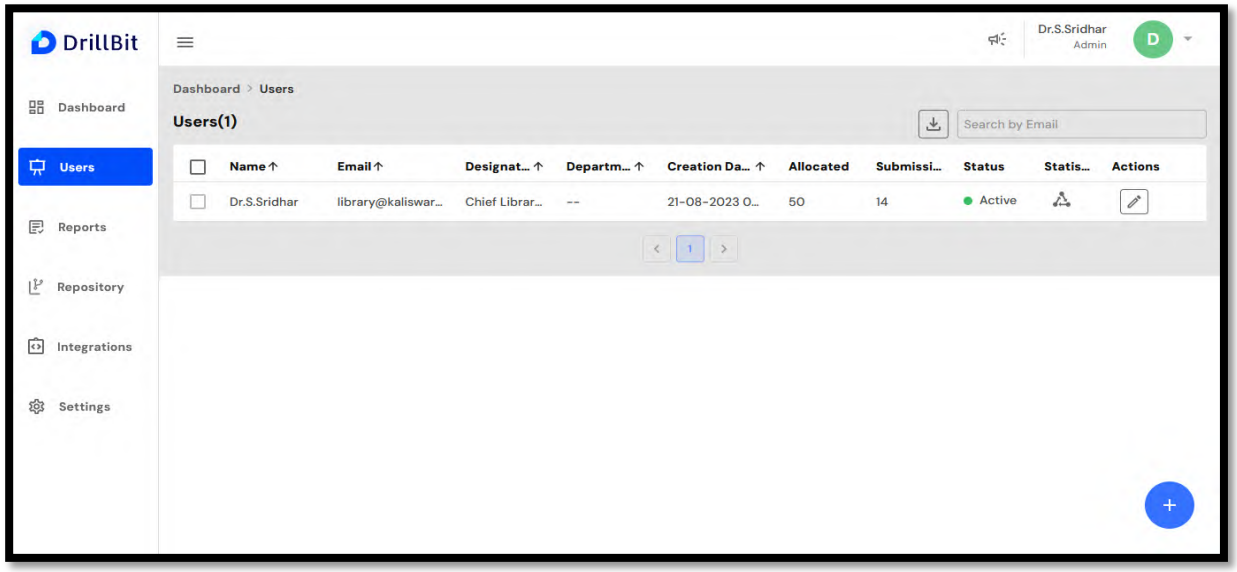

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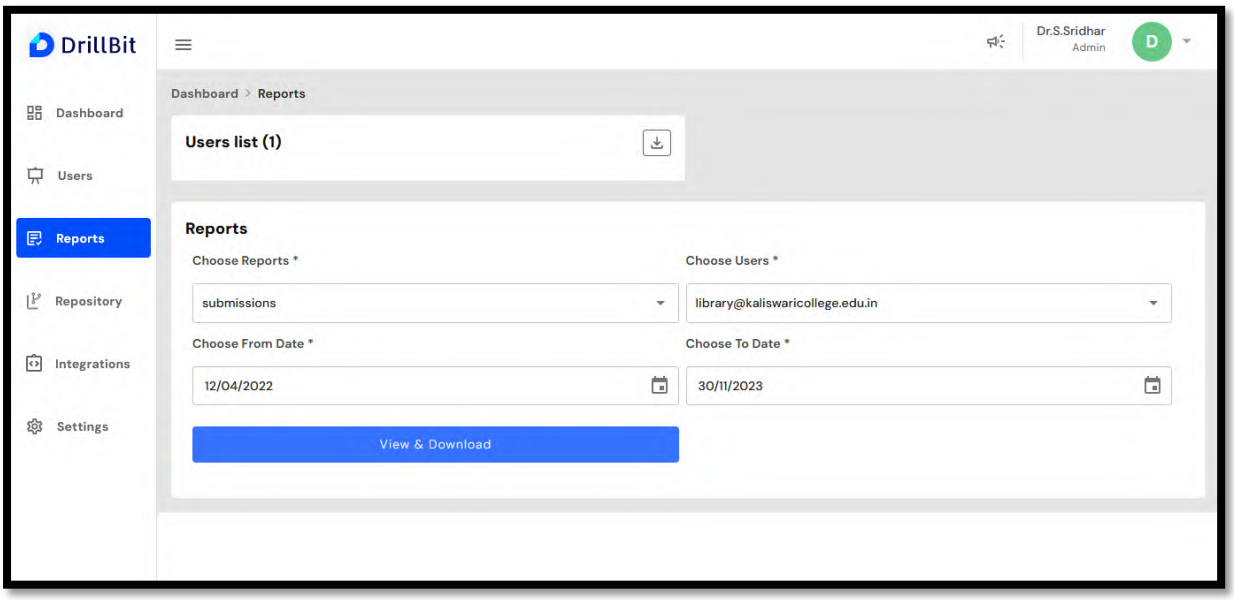

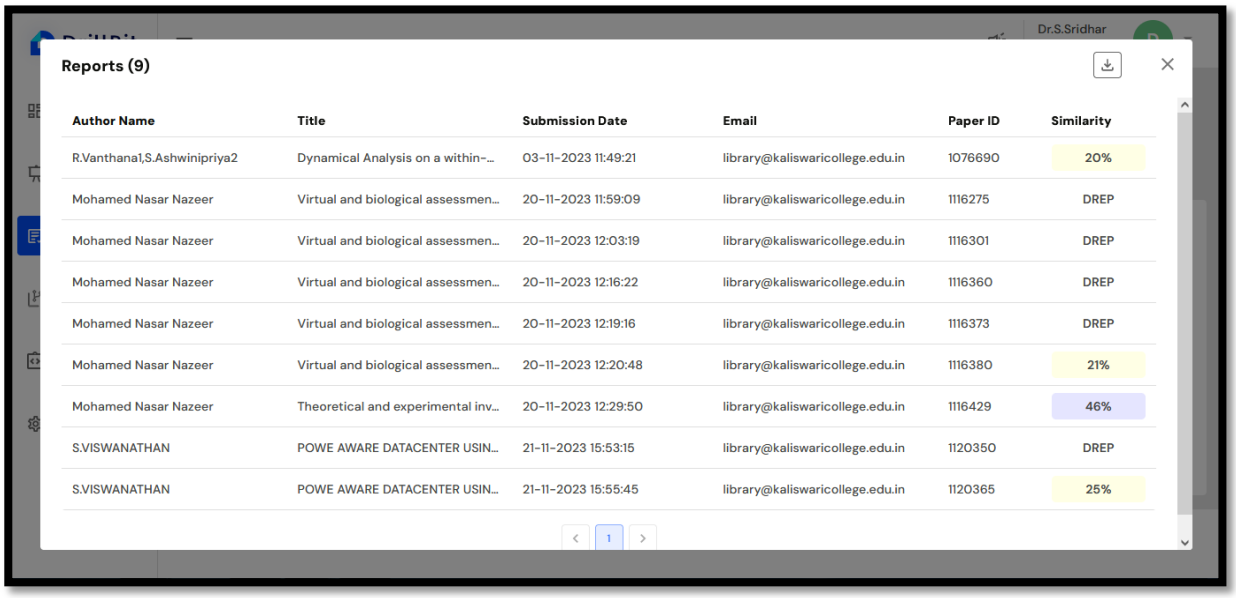

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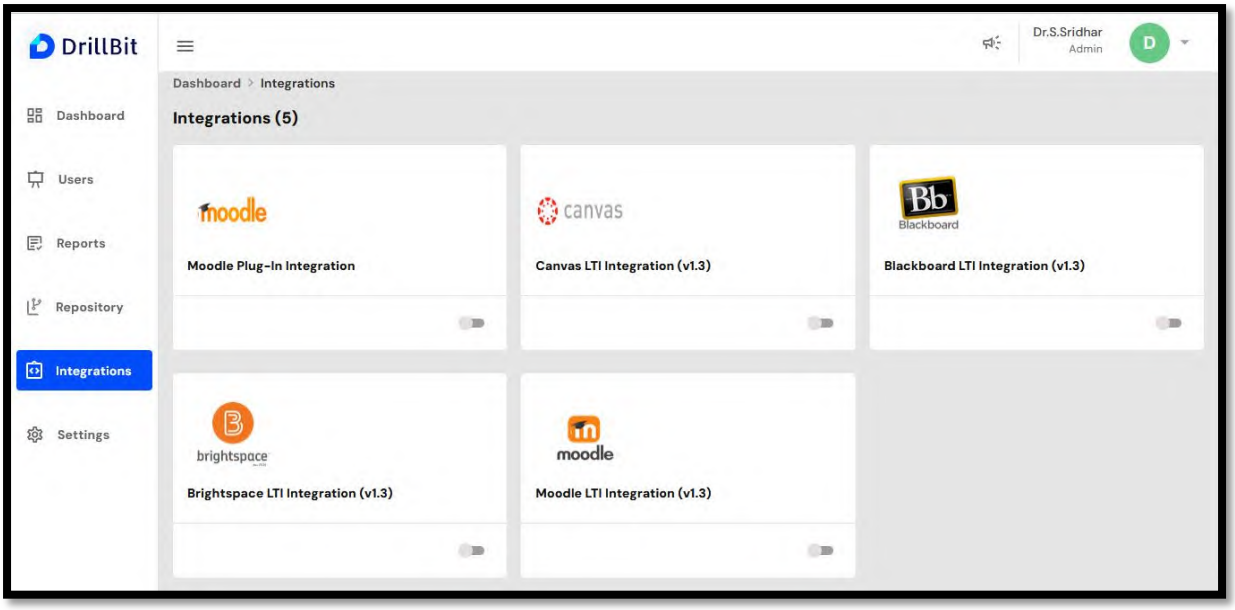

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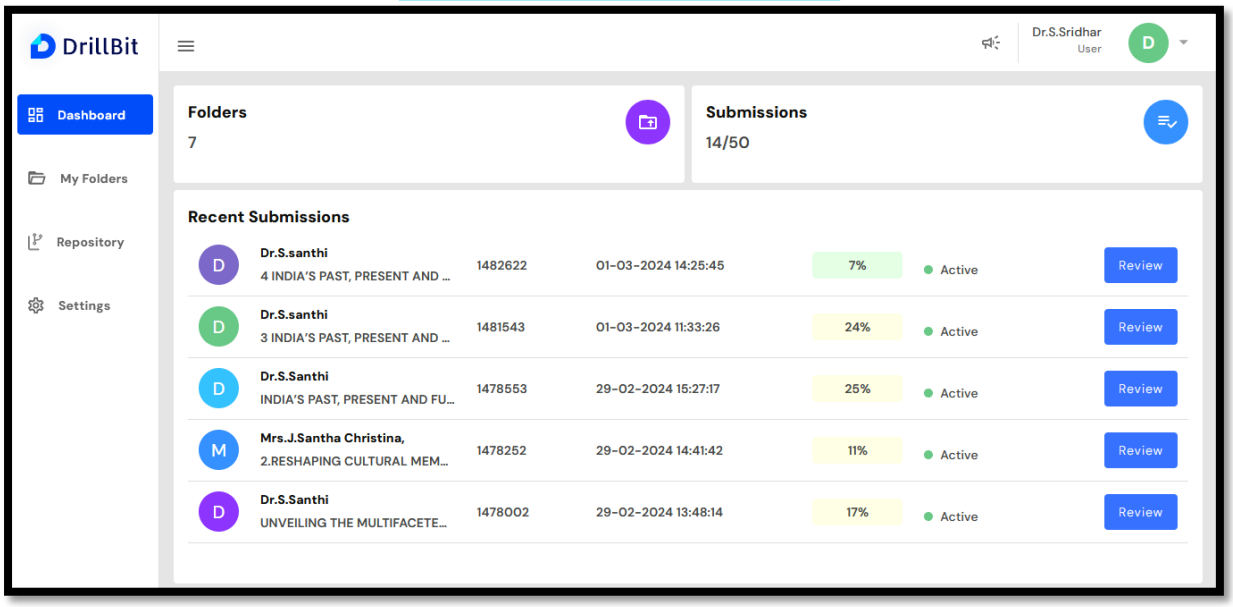

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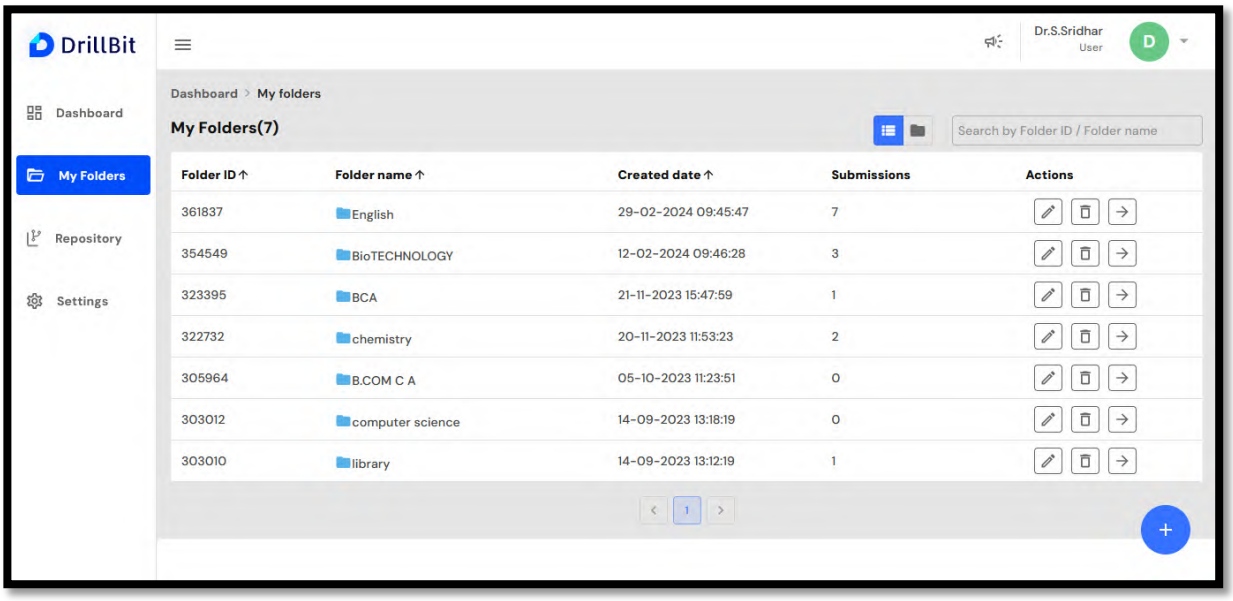

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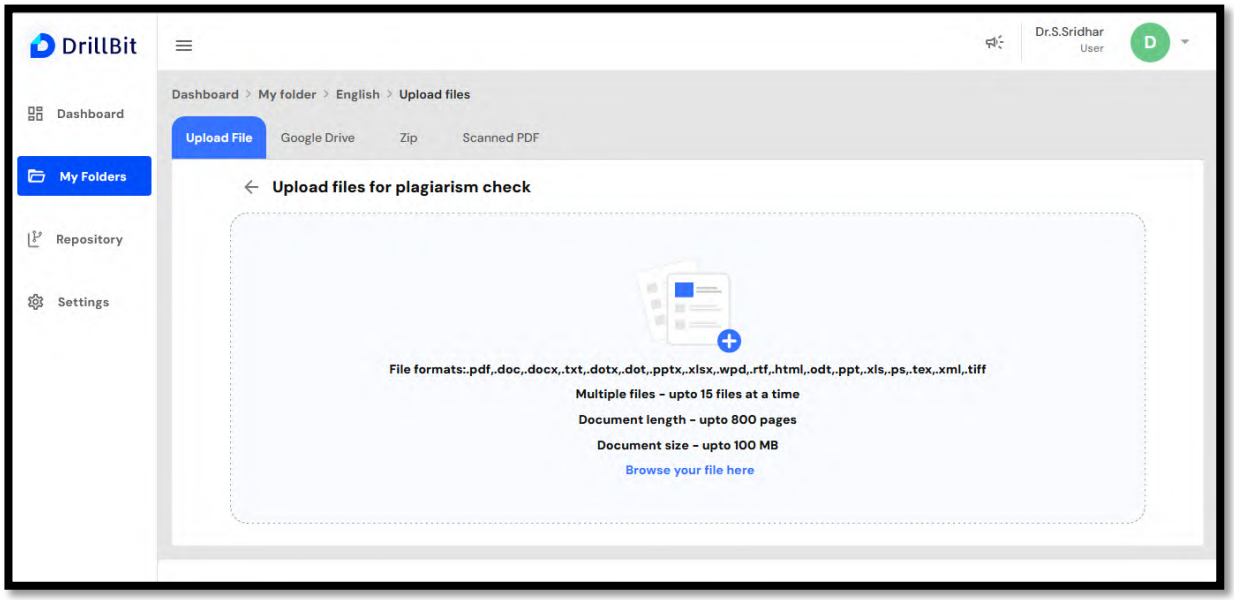

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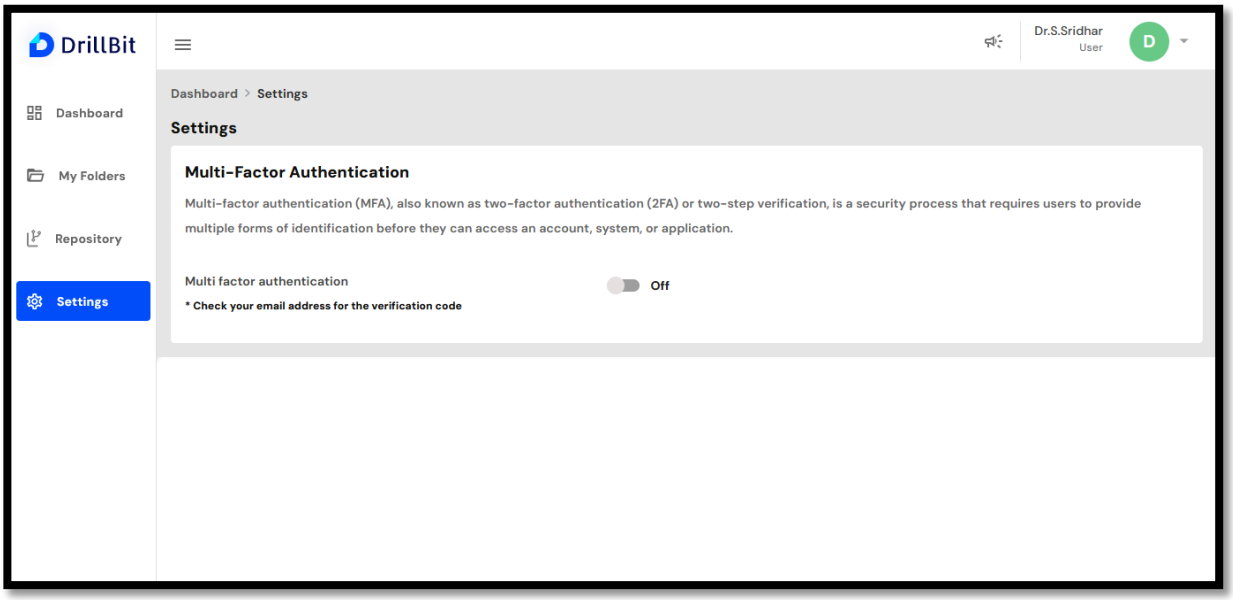

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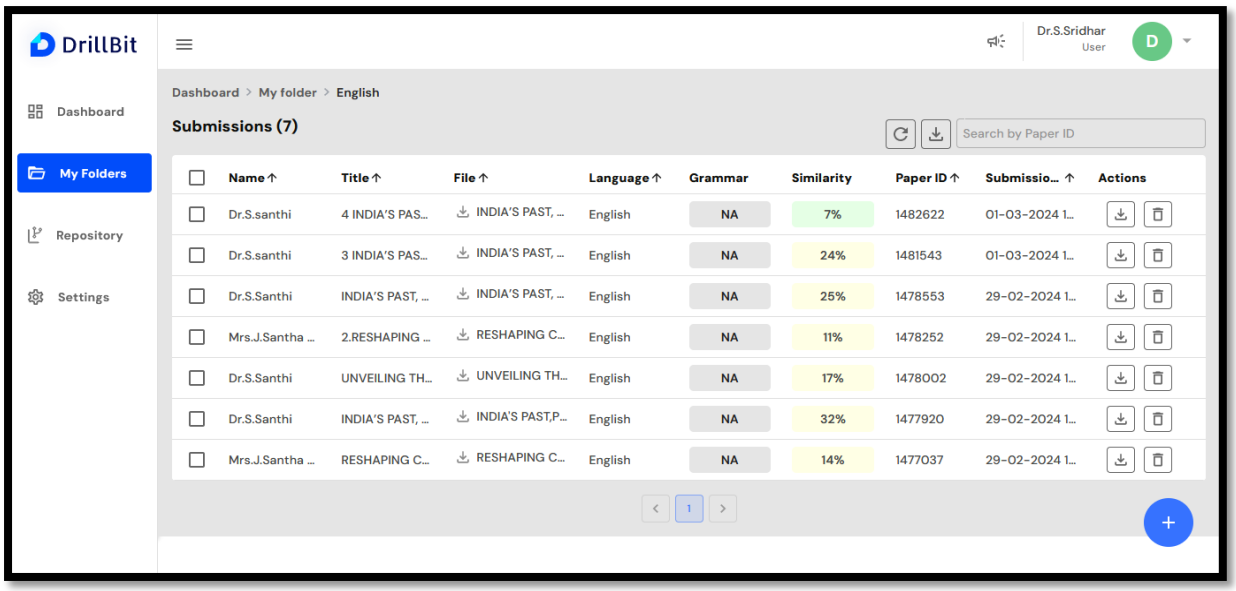

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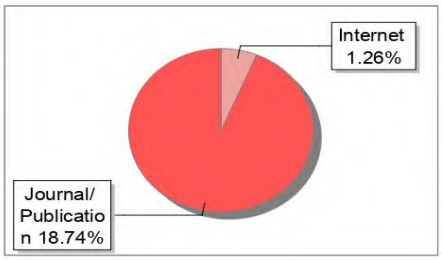

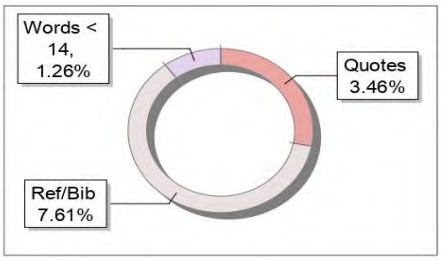

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Dynamical Analysis on a within-host mathematical model of COVID-19

R.Vanthana[1],S.Ashwinipriya[2]
[1,2]Assisstant Professor, Department of Mathematics, Sri Kaliswari College (Autonomous), Sivakasi-626130, India.

Abstract

A within-host mathematical model on the inflammatory mediators in COVID-19 is presented. Homotopy Perturbation Method (HPM) is discussed which is used to compute an approximate analytical expression for the concentrations of healthy type II Pneumocytes, infected type II Pneumocytesand viral load. The validity of HPM is analyzed using the function pde4, a function used to solve boundary value problems in MATLAB software. Graphical results confirm that (HPM) is in good agreement with the numerical solution adding to the accuracy and efficiency of (HPM) in finding the solution of the proposed model. The achieved results are applicable to the entire domain.

Keywords:*Mathematical Modeling, COVID-19, Nonlinear initial value problem, Homotopy Perturbation Method.*

1. Introduction

The outbreak of novel coronavirus in Wuhan, China marked the introduction of a virulent coronavirus into human society. The World Health Organization (WHO) named this novel corona viral pneumonia induced disease as Coronavirus disease (COVID-19) on Feb. 11, 2020. The causative agent of this disease is identified as Severe Acute Respiratory Syndrome coronavirus-2 (SARS-CoV-2).[1]. The transmission of SARS-CoV-2 from a person to another occurs either through droplet infection or by a direct contact with an infected host. Also, transmissions from asymptotic carriers have also been reported. In spite of several researches being carried around the world, we are still lacking effective treatment approaches and epidemiological control measures. So, in order to break the natural history of the disease, it is inevitable to identify the possible interventions that help in reducing the severity of the virus and the growth of infected cells. Therefore, it is crucial to determine the coaction of viral growth along with the host immune response in the form of inflammatory mediators. In this paper, an analytical expression is derived for the ratio of healthy type II Pneumocytes$S(t)$,infected type II Pneumocytes I(t),viral load V(t) against time t by applying the method of Homotopy Perturbation. These analytical expressions can be useful in predicting the course of the disease over time and the simulation of novel therapies under various mechanisms.

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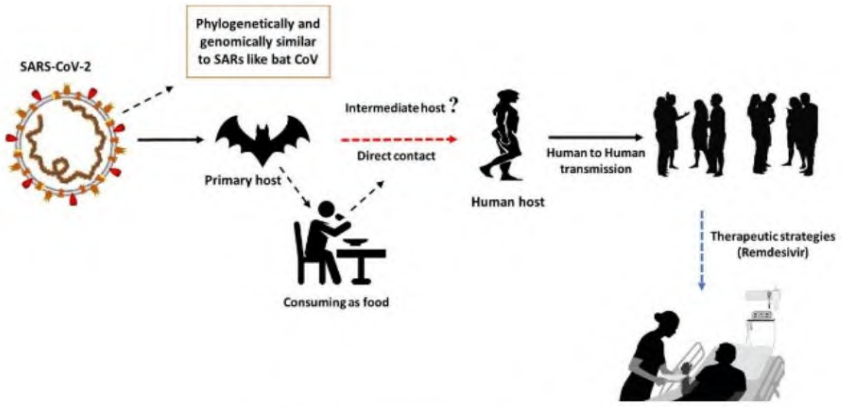

Fig. 1.Transmission of COVID-19

2. Mathematical Formulation of the Problem

Recently *D.K.K. Vamsi et al.* [2]formulated a mathematical model with reference to the pathogens that deals with the natural history of covid-19. This is a first of its kind. Up to our knowledge there is no analytical solution for this system of nonlinear equations. The model is denoted as

$$\frac{dS}{dt} = \omega - \mu S - \beta SV \qquad (1)$$

$$\frac{dI}{dt} = \beta SV - (d_1 + d_2 + d_3 + d_4 + d_5 + d_6)I - \mu I$$

$$\frac{dI}{dt} = \beta SV - DI - \mu I \qquad (2)$$

where $D = \frac{dI}{dt} = d_1 + d_2 + d_3 + d_4 + d_5 + d_6$

$$\frac{dV}{dt} = \alpha I - (b_1 + b_2 + b_3 + b_4 + b_5 + b_6)V - \mu_1 V$$

$$\frac{dV}{dt} = \alpha I - BV - \mu_1 V \qquad (3)$$

where $B = b_1 + b_2 + b_3 + b_4 + b_5 + b_6$

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Where $S(t)$ represents the healthy type II Pneumocytes, $I(t)$represent the infected type II Pneumocytes , and $V(t)$ represent the viral load . Let ω be the natural birth rate of type II Pneumocytes. Let the natural birth rate of the virus $V(t)$ be α and the natural death rate be μ_1.We suppose that infected type II Pneumocytes $I(t)$secrete virus $V(t)$that attacks the healthy type II Pneumocytes S(t) at rate β and the natural death rate of type II Pneumocytesbe μ . With the release of cytokines and chemokines IL-6 TNF-a, INF-a, CCL5, CXCL8, CXCL10, the infected Pneumocytes and the virus are removed at the rate $B$and Ddie at rate μ_1 respectively. The parameters ω , β , μ , α , μ_1,B,D are positive constants . The initial conditions for the above equations as t=0 are $S = S_t$, $I = I_t$, $V = V_t$ where $S(t)$represent the healthy type II Pneumocytes , $I(t)$represent the infected type II Pneumocytes , and $V(t)$ represent the viral load.

Table 1

Nomenclature

Parameters	Biological meaning
S	Healthy type II Pneumocytes
I	Infected Type II Pneumocytes
ω	Natural birth rate of Type II Pneumocytes
V	Viral load
β	Rate at which healthy Pneumocytes are infected
α	Burst rate of virus particles(rate at which infected cells release the virus particles)
μ	Natural death rate of Type II Pneumocytes
μ_1	Natural death rate of virus
$d_1, d_2, d_3, d_4, d_5, d_6$	Rates at which Infected Pneumocytes are removed because

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	the release of cytokines and chemokines IL-6 TNF-α , INF-α , CCL5, CXCL8 , CXCL10 respectively
$b_1, b_2, b_3, b_4, b_5, b_6$	Rates at which Virus is removed because of the release of cytokines and chemokines IL-6 TNF-α , INF-α , CCL5, CXCL8 , CXCL10 respectively

3. Analytical Solution for the within-host mathematical model on the inflammatory mediators

Homotopy Perturbation method is a combination of topology and classic perturbation techniques. It is implemented to compute an approximate solution to a system of nonlinear differential equations pertaining to the problem. The efficiency of the Homotopy perturbation method for handling and solving various non-linear structures problems can be found in [3-6]. Ji Huan He employed the Homotopy perturbation method to solve the Lighthill equation [7], the Duffing equation [8] and the Blasius equation [9]. The homotopy perturbation method makes use of a small imbedding parameter p due to which very fewiterations are required to achieve accurate result. The procedure for solving the non-linear differential equations, eqn. (1) -eqn. (3), by employing the method of homotopy perturbation is illustrated in Appendix A. The obtained results are as follows

$$S(t) = \frac{\omega}{\mu} + e^{-\mu t}(S_t - \frac{\omega}{\mu}) + \frac{\beta V_t \omega}{\mu B}(e^{-t(\mu+B)} - 1) + \frac{\beta V_t}{\mu + B}(e^{-t(2\mu+B)} - 1)(S_t - \frac{\omega}{\mu}) \quad (4)$$

$$I(t) = I_t e^{-t(D+\mu)} + \frac{\beta S_t V_t}{\mu + B - D}(1 - e^{-t(2\mu+B)}) \quad (5)$$

$$V(t) = V_t e^{-t(B+\mu)} + \frac{\alpha I_t}{D - B}(1 - e^{-t(D-B)}) \quad (6)$$

Where $S(t)$represents the healthy type II Pneumocytes, I(t) represent the infected type II Pneumocytes , and $V(t)$represent the viral load.

4. Numerical Simulation

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By implementing the Homotopy Perturbation Method, the non-linear differential equations governing the model (1)-(3) for the predetermined initial condition are established. These equations are illustrated numerically by making use of Matlab pdex 4 software which is presented in Appendix B. The obtained solutions in comparison with the analytical solutions admit a remarkable accuracy.

5. Result and Discussion

Fig. 2 illustrates the ratio of healthy type II Pneumocytes $S(t)$, infected type II Pneumocytes I(t),viral load V(t) against time t. Fig. 3-5 presents plot of the ratio of healthy type II Pneumocytes$S(t)$ against time t by varying parameters $R1$,$R2$,$R3$ respectively. From Fig 3, it can be noted that the ratio of healthy type II Pneumocytes $S(t)$ increases steadily due to the increase in natural birth rate of type II Pneumocytes. From Fig. 4, it can be seen that there is an deterioration in the ratio of healthy type II Pneumocytes $S(t)$. This is due to the increase in rate at which healthy Pneumocytes are infected.Fig. 5 depicts that there is an decline in the ratio of healthy type II Pneumocytes $S(t)$ which is a consequence of the natural death rate of these cells. . Fig. 6-7 presentsplot of the ratio of infected type II Pneumocytes $I(t)$ against time t by varying parameters $R3$,$R4$ respectively. From Fig. 6, it can be observed that the ratio of infected type II Pneumocytes $I(t)$ decreases steadily due to the increase in natural death rate of type II Pneumocytes. From Fig. 7, it can be noted that when the infected type II Pneumocytes are removed from the host the ratio of infected type II Pneumocytes $I(t)$ decreases. From this it can be inferred that the immunization drugs play a pivot role in stopping the spread of the infected cells. Fig. 8- 10 represents plot of the ratio of viral load $V($ $t)$ against time t by varying parameters $R5$,$R6$,$R7$ respectively. From Fig. 8, it can be noted that when the rate of removal of the virus from the host is high the ratio of the viral load decreases. From Fig. 9, it can be seen that ratio of the viral load $V(t)$decreases as the death rate of the virus increases. From Fig. 10, it can be observed that ratio of the viral load $V(t)$ increases when the rate of release of the virus from the infected cells is maximum. The higher the infected cells, the higher the viral load. Therapeutic agents which acts to improve the response of the host immune system in reducing the number of infected cells and viral load can be administered.

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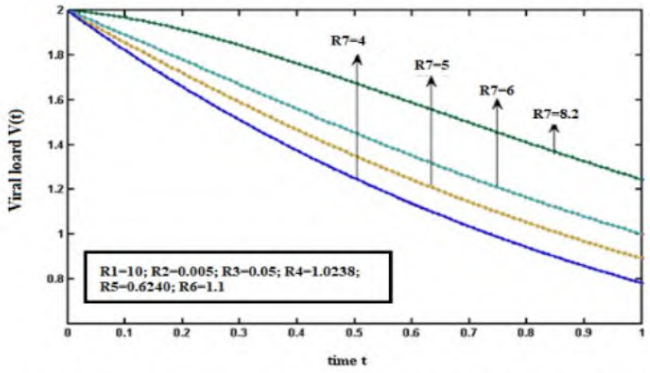

Fig. 10. Plot of viral load V(t) versus time. The correlation is assessed for Eq. (3) with distinct values of the parameter R7 and the allotted values of other parameters R1 = 10; R2 = 0.005;R3 = 0.05; R4 = 1.0238; R 5 = 0.6240; R6 = 1.1.The annotation to the graph: solid line constitutes the Eq. (3) and dotted line constitutes the numerical solution.

6. Conclusion

In this paper, HPM is employed to attempt the solution of the model. Numerical simulations were performed to compare the analytical results obtained by HPM with numerical results. The results of the simulations were illustrated graphically. The results show that the analytical solution is in good agreement with the numerical results and produced accurately the same behavior. A clear conclusion can be drawn that HPM is highly reliable in finding the solution of a nonlinear differential Equation.

Author Contributions

S. Ashwinipriya: Data curation, Software, Formal analysis, Visualization, Writing - original draft.

R.Vanthana: Methodology, Resources, Conceptualization, Investigation, Writing - review & editing, Project administration, Supervision, Validation.

Conflict of interest

The authors declare that they have no conflict of interest.

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$$p^1 : \frac{dy_1}{dt} + ay_1 - bx_0v_0 = 0 \qquad \text{(A.11)}$$

$$p^1 : \frac{dv_1}{dt} + kv_1 - cy_0 + dx_0v_0 = 0 \qquad \text{(A.12)}$$

Appendix B: Matlab/Scilab program to find the numerical solution of the eqns. (1)-(3):

```
function main1

options= odeset('RelTol',1e-6,'Stats','on');

Xo = [0.5;0.4;2];
tspan = [0,1];

tic

[t,X] = ode45(@TestFunction,tspan,Xo,options);

toc

figure

holdon

%plot(t, X(:,1),'g')

%plot(t, X(:,2),'r')

%plot(t, X(:,3))

return

function [dx_dt]=TestFunction(t,x)

R1=10;R2=0.005;R3=0.05;R4=1.0238;R5=0.6240;R6=1.1;R7=8.2;
dx_dt(1)=(R1-(R2*x(1)*x(3))-(R3*x(1)));
dx_dt(2)=(R2*x(1)*x(3))-((R4+R3)*x(2));
dx_dt(3)=(R7*x(2))-(R5*x(3))-(R6*x(3));
dx_dt = dx_dt';

return
```

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