Global Journal of Pure and Applied Mathematics.
ISSN 0973-1768 Volume 11, Number 4 (2015), pp. 2581-2587

http://www.ripublication.com

Mathematical Modelling For Chemotherapy Of Tumor Growth With Aspect Of Biological Stoichiometry

Deep Shikha Dixit[1], Deepak Kumar[2], Sanjeev Kumar[3], Rajesh Johri[4]

1. Department of Mathematics, CET IILM, Gr. Noida. shikha0115@gmail.com
2. Department of Mathematics, FET, Manav Rachna International University, Faridabad, Haryana (India) deepakman12@gmail.com
3. Department of Mathematics, I.B.S. Khandari Agra, Dr. B.R.Ambedkar University, Agra, U.P.(India).
4. Department of Mathematics, Agra College, Agra Dr. B.R.Ambedkar University, Agra, U.P.(India).

Abstract:

The model presented in this work gives a way of tumor treatment in which we apply chemotherapy on parenchyma cells to block phosphorus uptake by tumor cells. To describe this model we use system of non-linear delay differential equations. Mathematical and numerical analysis of the model show that this way of treatment may lead to a significance reduction in tumor size.

Introduction:

Despite a greatly expanded knowledge base, post-occurrence cancer survival rates have shown only modest improvements in recent decades. Thus new approaches are needed that can integrate the diverse body of knowledge in this field to yield a better understanding of cancer and improve available therapies. One increasingly important emphasis in cancer biology is to consider a growing tumor as a complex ecological and evolutionary system and this is called “Biological-Stoichiometric” (Sterner et. al. 2002). By definition biological-stoichiometric is the study of the balance of energy and multiple chemical elements in biological systems. A key idea in biological stoichiometry is the growth rate hypothesis, which states that variation in the carbon: nitrogen: phosphorus stoichiometry of living thing is associated with growth rate because of the elevated demands for phosphorus – rich ribosomal RNA, a requirement for rapid growth (Elser et. al. 2000). Synthesizes studies in the cancer literature to test

the growth rate hypothesis, consistent with its predictions, rapidly growing tumors have elevated ribosome content, key oncogenes are closely affiliated with regulation of ribosome biogenesis, and tumor development has physiological impacts on patient phosphate metabolism. He also described a new eco-evolutionary model of tumor dynamics that incorporates stoichiometric mechanisms.

According to Nagy D. J. (2004), tumors are both an ecological community and an integrated tissue. In his work he addressed natural selection's role in tumor evolution by developing and exploring a mathematical model of a heterogeneous primary neoplasm, and also his model suggests that parenchyma cell diversity can be maintained by a tissue-like integration of cells specialized to provide different services.

Kuang Y. et.al. (2004) integrated the elements namely natural selection driven by competition for resources, especially phosphorus into mathematical models consisting of three or more nonlinear delay differential equations. These models track mass of healthy cells within a host organ, mass of parenchyma (cancer) cells of various types and the number of blood vessels within the tumor. Mathematical and numerical analysis of these models show that tumor population growth and ultimate size are more sensitive to total phosphorus amount than their growth rates are. This paper also introduced these concepts to cancer biologists, explore the utility of applying these ideas to a model of tumor dynamics, and to describe some potential implications of a stoichiometric view for preventive and therapeutic strategies in cancer.

Our work in the same direction here we applying chemotherapy on parenchyma cells to reduce the size of the tumor or may prevent the tumor from reaching a lethal size. The goal in cancer therapy is to assure that the host (patient) wins in this ecological competition or, at the least, that there is a long-term stable coexistence between the two in which the host maintains an acceptable level of health.

Mathematical Model:

In this paper we enhance the previous model developed by Kuang Y. et al. (2004) by applying chemotherapy on parenchyma cells(y) (i.e. applying drugs capable of selectively blocking phosphorus uptake by tumor cells) to reduce the size of the tumor or reaching from a lethal size.

Here, the variables x(t), y(t) and z(t) represents the mass of healthy cells, mass of tumor cells and mass of tumor micro vessels respectively at time t.

For healthy cells, the phosphorous content on a kg. of healthy cells, m_1-per capita growth rate without crowding effects, m_2-healthy cells proliferation rate at maximum per capita, d_1-healthy cells suffer a constant per capita mortality.

$$\frac{dx}{dt} = m_1 x - m_2 \left(x + y + z \right) - d_1 \qquad (1)$$

For cancer cells, m_3-per capita growth rate without crowding effects, m_4-cancer cells proliferation rate at maximum capita, d_2- cancer cells suffer a constant per capita mortality.

$$\frac{dy}{dt} = ym_7m_3 - d_2m_4 \quad y+z \quad -G \quad t \quad y \tag{2}$$

Where, chemotherapy term *G(t)*, on parenchyma (tumor) cells and k is the value for chemotherapy on. It controls the limiting phosphorus uptake by cancer cells.

$$G(t) = \begin{matrix} k, & t \in chemo \\ 0, & otherwise \end{matrix}$$

Mass of tumor micro vessels, m_5-new micro vessels arise from activated VEC precursor cells within the tumor stroma at per capita if there is no phosphorus limitation; d_3- tumor micro vessels suffer a constant per capita mortality

$$\frac{dz}{dt} = m_5y - d_3z \tag{3}$$

In particular whenever $m_7<1$, then the maximum proliferation rate of tumor cells becomes m_7, where μ represents the mass of cancer cell that one unit of blood vessels can just barely maintain, and l measures sensitivity of tumor tissue to lack of blood.

$$m_7 = \frac{l(z-\mu y)}{y} \tag{4}$$

As we know that patients vary in size and that organ and tumor carrying capacities vary in the same direction so we take our analysis on only one generic patient, a person with a body mass of about 70 kg and about 700 gm of total body phosphorus. For concreteness we assume that the tumor arises in the lung, and further values are taken as:

Parameter Estimations:

m_1	**0.99**
m_2	**0.06**
m_3	**.0099**
m_4	**0.6**
m_5	**0.0045**
m_6	**0.02**
m_7	**0.350**
μ	**0.05**
l	**100**
d_1	**1**
d_2	**1**
d_3	**0.2**
$x(0), y(0), z(0)$	0.01,0.01,0.001

Result:

Here we developed a mathematical model for applying chemotherapy on parenchyma cells to block phosphorus uptake by tumor cells. The numerical procedure used to approximate the system of non-linear delay differential equations being approximate using MATLAB 6.0, to solve the non-linear delay differential equations.

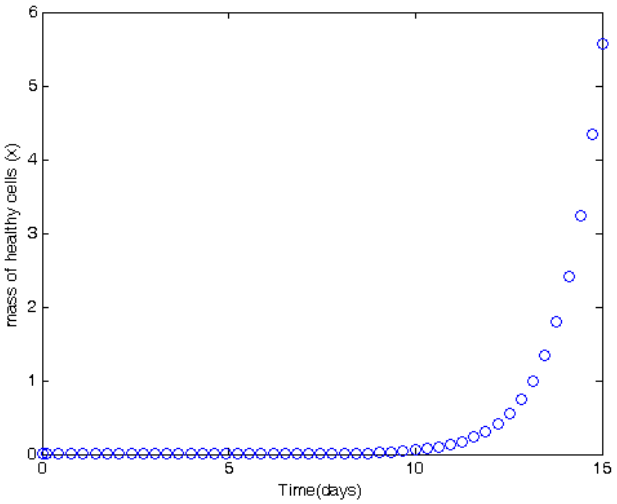

Figure (A) represents that mass of healthy cells with respect to time (days). At initial stage the mass of healthy cells is 0.00(min.), but it is growing after 10 days due to apply chemotherapy on parenchyma cells to block phosphorus uptake by tumor cells. Therefore the numerical solution shows that the mass of healthy cells is increasing from 0.00 to 5.6 because chemotherapy is working to block phosphorus uptake by tumor cells.

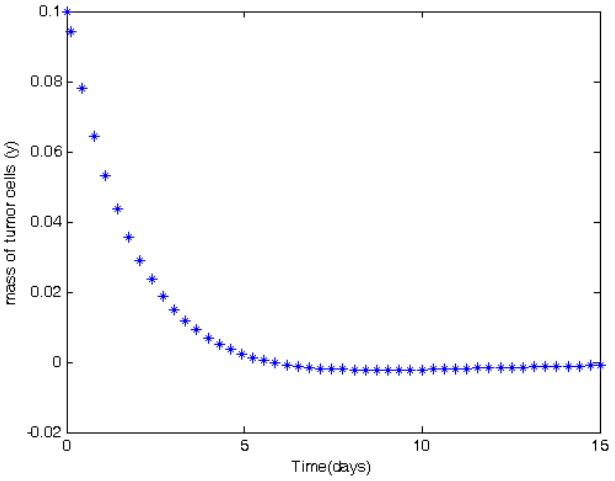

Figure (B) represents that mass of tumor cells with respect to time (days). At initial stage the mass of tumor cells is 0.1 (max.), but it is decreasing due to apply

chemotherapy on parenchyma cells to block phosphorus uptake by tumor cells. Therefore the numerical solution shows that the mass of tumor cells is decreasing from 0.1 to 0 with respect to time because chemotherapy is working to block phosphorus uptake by tumor cells.

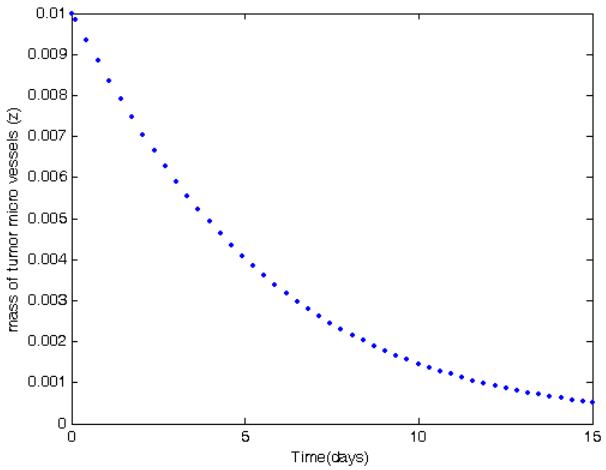

Figure (C) represents that mass of tumor micro vessels with respect to time (days). At initial stage the mass of tumor micro vessels is 0.01(max.), but it is decreasing due to apply chemotherapy on parenchyma cells to block phosphorus uptake by tumor cells. Therefore the numerical solution shows that the mass of tumor cells is decreasing from 0.01 to 0.001 with respect to time because chemotherapy is working to block phosphorus uptake by tumor cells.

Discussion:

To describe this model we use here non-linear delay differential equations. According to model, in which organ phosphorus content is held constant. From previous work done, we know the fact that dietary phosphorus restriction alone is unlikely to benefit our patient. While it is true, according to Elser J. J. (2004)'s model dietary restriction of phosphorus can reduce tumor growth and ultimate size, both ultimate tumor size and organ size change in the same direction – in fact, almost proportionally. Therefore restricting phosphorus damages the healthy organ as much as it does the tumor. So we try to reduce tumor phosphorus uptake without affecting phosphorus availability to healthy cells.

As we know chemotherapy is a common therapy for oncology patients, so here we apply same therapy for our patients. Here we apply chemotherapy on parenchyma cells (i.e. applying drugs capable of selectively blocking phosphorus uptake by tumor cells). By this we try to reduce the size of the tumor without less affecting the healthy cells. Therefore in our model we particularly, take $m_7 < 1$ it reduces ultimately tumor size while maintain the organ at a healthy size.

However, we caution that the model presented here was not designed for direct clinical application. Much more specific information and rigorous comparisons

between model results and actual tumors is required when applied to treatment decisions in any way. Although it may give rise to useful tools that oncologists can use to help decide the proper course of chemotherapy for specific patients. Our work suggests that in future look for some more ways to selectively reduce the rate of phosphorus uptake by tumor cells. The advantage of such a treatment is that it may dramatically reduce tumor size while maintain the organ at a healthy size.

REFERENCES:

[1] Merlo LMF, Pepper JW, Reid BJ, Maley CC (2006) Cancer as an evolutionary and ecological process. Nat Rev Cancer 6: 924-935.

[2] Sterner RW, Elser JJ (2002) Ecological Stoichiometry: The Biology of Elements from Molecules to the Biosphere. Princeton, N.J.: Princeton University Press.

[3] Elser JJ, Sterner RW, Gorokhova E, Fagan WF, Markov TA, et al (2000) Biological stoichiometry from genes to ecosystems. Ecol Lett 3: 540-550.

[4] Elser JJ, Kuang Y, Nagy J (2003) Biological stoichiometry of tumor dynamics: an ecological perspective. Bioscience 53: 1112-1120.

[5] Loladze I, kuang Y, Elser JJ (2000) Stoichiometry in producer-grazer systems: Linking energy flow with element cycling. Bull. Math. Biol., 62, 1137-62.

[6] Nagy JD (2003) a Competition and Natural Selection in Mathematical model of Cancer. Bull. Math. Biol., 66, 663-687.

[7] Elser JJ, Kyle MM, Smith MS, Nagy JD (2007) Biological Stoichiometry in Human Cancer. Plos One 2(10) e1028.

[8] Elser JJ, Acharya R, Kyle M, Cotner J, Makino W, et al. (2003) Growth rate stoichiometry couplings in diverse biota. Ecol Lett 6: 936-946

[9] Kuang Y, Nagy JD, Elser JJ (2004) Biological Stoichiometry of Tumor Dynamics: Mathematical Models and Analysis. Disc. and Cont. Dyna. Sys. 4, 221-240.

[10] Ahrean T. S., Staff R. T., Redpath T. W., and Semple S. I. K., The Effect of Renal Variation Upon Measurements of Perfusion and Leakage Volume in Breast Tumors, *Physics in Medical and Biology*, **49**, (2004), 2041-2051.

[11] Jackson, T.L. (2002): Vascular tumor growth and treatment: consequences of polyclonality, competition and dynamic vascular support. *J. Math. Biol.*, **44**, 201-26.

[12] Kuang, Y. (1993): *Delay differential equations with applications in population dynamics.*New York, Academic Press.

[13] Li, J., Y. Kuang and B. Li (2001): Analyses of IVGTT glucose-insulin interaction models with time delay, *Discrete Contin. Dynam. Systems, B*, **1**, 103-24.

[14] Deepak Kumar and Sanjeev Kumar (2006): A Mathematical Model for the Immune System Competition-the effect of Replication-competent virus dosages. Acta Ciencia Indica, Vol. XXXII M, No. 2, 543.

[15] Deepak Kumar and Sanjeev Kumar (2006): A Computational Model for the Interaction between cell Density and Immune Response. Acta Ciencia Indica, Vol. XXXII M, No. 2, 549.

[16] Deepak Kumar and Sanjeev Kumar (2010): A Mathematical Model of Radio immunotherapy for Tumor Treatment. African Journal of Mathematics and Computer Science Research Vol. 3(6), June 2010, pp. 101–106.

[17] Deep Shikha dixit, Deepak Kumar, Sanjeev Kumar, Rajesh Johri (2011): A Mathematical model of vascular tumor with chemotherapy drug concentration at nano-scale. International Journal of Applied Mathematics and Applications, 3(1), June 2011, pp. 77-83.

[18] Shashi Kant, Sanjeev Kumar and Deepak Kumar (2011): A Mathematical Model of Tumour Growth with a Specific Dose of Il-4 (Interleukin-4). Mathematical Modelling and Applied Computing, Volume 2 NUMBER 1. pp. 1-8.