RESEARCH PAPER | Mathematics | Volume : 4 | Issue : 2 | Feb 2014 | ISSN - 2249-555X

A Mathematical Model of Chemotherapeutic Drug for Tumor Treatment

KEYWORDS: tumor growth, mathematical modeling, selenium with the combination of Adriamycin, partial differential equations.

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ABSTRACT *This work considers a model that represents the procedure for tumor treatment, which consists tumor cell energy and specific dose of selenium with the combination of Adriamycin. The tumor cell energy depends upon tumor cell density and the selenium with the combination of Adriamycin is a specific drug that works against tumor cell energy. The problem in the form of partial differential equations for the tumor cells density, tumor cell energy and the effect of selenium with the combination of Adriamycin. The result of this work suggests that the tumor cell energy decrease by the effect of selenium with the combination of selenium with the combination of Adriamycin, if tumor cell energy decreases then the size of tumor reduces.*

Introduction:

Main focus on the work because combination of selenium enhanced chemotherapeutic effect of Adriamycin in tumor cells beyond that seen with the Adriamycin(Doxorubicin) used alone. Selenium is a natural health product widely used in the treatment and prevention of cancers, but not good for large chemotherapeutic treatment of tumor. The energy in all cells originates from the energy of the sun's light quanta, which is convicted by photosynthetic plants into cellular molecules. These plants are used as food sources by various microorganisms and animals. Life is an energy process. It takes energy to operate muscles, extract wastes, make a new cell, heal wounds, even to think. It's in an organism's cells where all this energy is spent. In some cells, as much as a half of a cells energy output is used to transfer molecules across the cell membrane. Cell movements require energy and thousands of energy-hungry chemical reactions go on in every living cell, every second, every day. The casual agents are certain chemicals, radiation, and viruses that behave as mutagens by acting at the level of DNA. However, it has also been proved that cancer is a genetic disease caused by multiple mutations within the DNA of cells. The researchers [3] have discovered that an apparently nontoxic cellular "energy blockers" can eradicate large liver tumors grown, in rats. Liver cancer usually isn't detected in people until it's difficult or impossible to treat, and many other aggressive cancers spread to the liver, so we need more treatment options.

Martin et. al. [1] a quadruple drug combination consisting of a triple-drug combination of N-(phosphonacetyl)-L-aspartate (PALA) + 6-methylmercaptopurine riboside (MMPR) + 6-amino-nicotinamide (6-AN), designed to primarily deplete cellular energy in tumor cells, + selenium with the combination of Adriamycin (Adria) yielded significantly enhanced anticancer activity (i.e., tumor regressions) over that produced by either Adria alone at maximum tolerated dose (MTD) or by the triple-drug combination, against large, spontaneous, autochthonous murine breast tumors. selenium with the combination of Adriamycin is a type of antibiotic used specifically in the treatment of cancer. It interferes with the multiplication of cancer cells and slows or stops their growth and spread in the body. Stolfi et. al. [2] this report describes a highly active chemotherapeutic drug combination. This quadruple drug combination, administered on a 10-11-day schedule, produced an impressive partial tumor regression rate of 67% of large, spontaneous, autochthonous, murine breast tumors and a tumor regression rate of 74% of first-passage transplants of the spontaneous breast tumors.

Selenium with the combination of Adriamycin, which is administrated intravenously only. It is most commonly used in treatment of all cancers (Breast, Stomach, Lymphomas etc.). Selenium with the combination of Adriamycin is chemotherapy drug that interrupts the cell cycle, effectively cell growth. Selenium with the combination of Adriamycin degrades rapidly in solution; a fluorometric method was developed to determine the precise dose use in treatments. But selenium with the combination of Adriamycin also has more serious side effects that limit the amount you can safely take. At a certain level, selenium with the combination of Adriamycin increases the risk of heart damage. The selenium with the combination of Adriamycin works by impairing DNA synthesis, a crucial feature of cell division, and this is able to target rapidly dividing cells. Selenium with the combination of Adriamycin is a very serious anticancer medication with definite potential to do great harm as well as great good. It used alone or in combination with other chemotherapy drugs. Ward and King [10] consider the effect of cellular material as well, mainly because it is very simple to construct an analogous model to that of Ward and King [9] for monolayer cultures, so that a direct comparison of the effect of drugs on the two types culture can be made the approach used in this model of Ward & King [12], which assumes source of cellular material outside a 3-dimensional monolayer case. Anderson et. al. [13] works to examine fluid flow through the theoretical network structures.

2. Our model:

Mathematically, for an untreated tumor the work equation may be reasonably quantified by a single partial differential equation

$$\frac{\partial c}{\partial t} = \nabla . J + \lambda c \qquad (1)$$

in which c(x,t) designates the tumor cell density and λ denotes the cell proliferation rate. Where $J = D\nabla\mu(c)$, the gradient of the potential μ produces a flux J is proportional to $\nabla\mu$. The D is Fickian diffusion coefficient represent the active motility of tumor cells, which in this derivation may depend on x, t and c. The tumor spread is assumed to be spherically symmetric in this model, and x measures the distance from the center.

$$\frac{\partial c}{\partial t} = \nabla . [D\nabla\mu(c)] + \lambda c \qquad (2)$$

Associate with a spatial distribution of cells, an energy den-

Volume : 4 | Issue : 2 | Feb 2014 | ISSN - 2249-555X

sity n(c), which is an internal energy per unit volume of an evolving spatial pattern so that the total energy N(c) in a volume is given by

$$N(c) = \int_V n(c)dx \qquad (3)$$

The small variation in energy δN which is the work done in small variety states by an amount δc, is the variation derivative, $\delta N/\delta c$ which define a potential $\mu(c)$. Therefore

$$\mu(c) = \frac{\delta N}{\delta c} = n'(c) \text{ (Because } \delta c \to 0\text{)} \qquad (4)$$

The internal energy density is usual quadrate with $n(c) = c^2/2$. In this context, I see that tumor cell energy depend on tumor cell density thus I get $\mu(c) = c$. Thus, I choose the following functional form for tumor cell c as discussed by in Burgess et al.[7]. I set:

$$c(x,T) = \frac{N_0 e^{\lambda(t_0+T)} e^{-x^2/4D_0}}{8(\pi D_0)^{3/2}} \qquad (5)$$

I find the initial and boundary condition for the selenium with the combination of Adriamycin resistance tumor cell density is determined as

$c = c_0(x)$ at t=0

$c = c_{\max}$. at x=0

$c = c_*$ at x=1

Now introduce the dose of selenium with the combination of Adriamycin bind with cells and it can prevent to repair of DNA. The selenium with the combination of Adriamycin can be use against repair of DNA of tumor cells; the term α is the effect of selenium with the combination of Adriamycin on tumor.

Such that

$$\frac{\partial c}{\partial t} = \nabla(D\nabla c) + \lambda c - \alpha c \qquad (6)$$

3. Numerical result:

The parameters

D tumor diffusion coefficient	54×10^{-4} mm²/h
λ net proliferation rate	50.4×10^{-4} /h
N_0 initial size of tumor at point of source	1.19×10^{6} cells
t_0 time to grow from point source to presentation	1.18×10^{4} h

To solve the partial differential equation, I use the Matlab 6.0, a partial differential equation solver. In this result, I see that the tumor cell density is going to decrease as well as the effect of selenium with the combination of Adriamycin is increases. It shows that if tumor cell density decreases with the effect of selenium with the combination of Adriamycin then tumor cell energy decreases with the dose of selenium with the combination of Adriamycin because tumor cell energy is depend upon the tumor cell density.

Figure 1: (a) showing the tumor cell density without effect of selenium+adriamycin and distance (0 to 1mm) from the center of the tumor and time (0-100h)

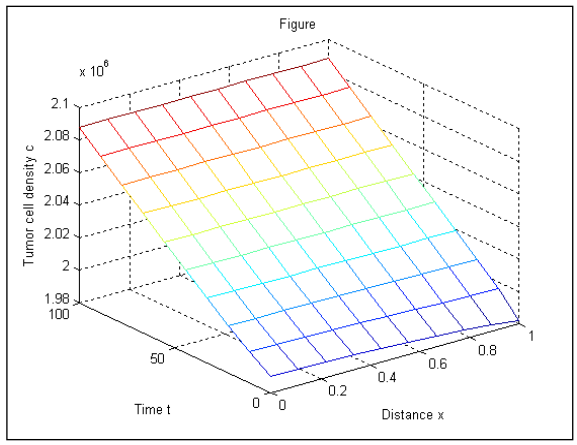


Figure 1(a) showing the tumor cell density without effect of selenium+adriamycin and distance (0 to 1mm) from the center of the tumor and time (0-100h)

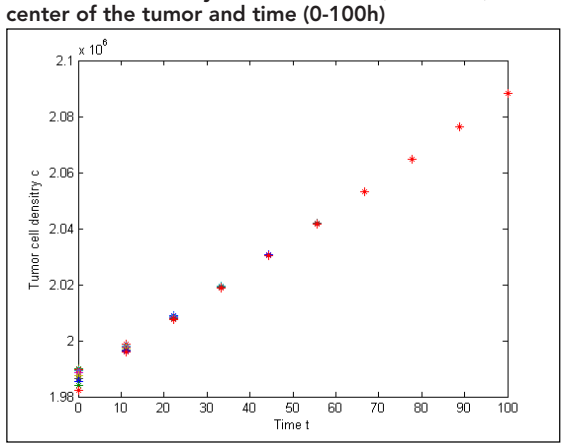


Figure 1: (b) showing the tumor cell density with time without effect of selenium+adriamycin time (0-100h)
Figure 1 shows the 3D and 2D representation in the above diagrams.

The figure 1 shows the surface plot tumor cell density with respect to time T and radius x. I consider the time 0 to 100 h and radius 0 to 1 mm. I analyzed the growth of tumor cell density in above figure shows the initially, tumor cell density is cells at center of tumor and cells at the boundary of the tumor. After the 100h the tumor cell density is almost same at the center and boundary of the tumor, without the effect of selenium with the combination of Adriamycin. The figure shows at initially max. at the center of tumor but it is less at the boundary.

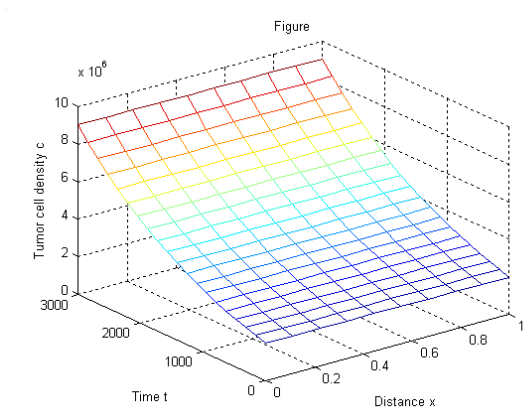


Figure 2: (a) showing the tumor cell density without effect of selenium+Adriamycin $\alpha = 0/h$ and distance

Volume : 4 | Issue : 2 | Feb 2014 | ISSN - 2249-555X

(0 to 1mm) from the center of the tumor and time (0-3000h)

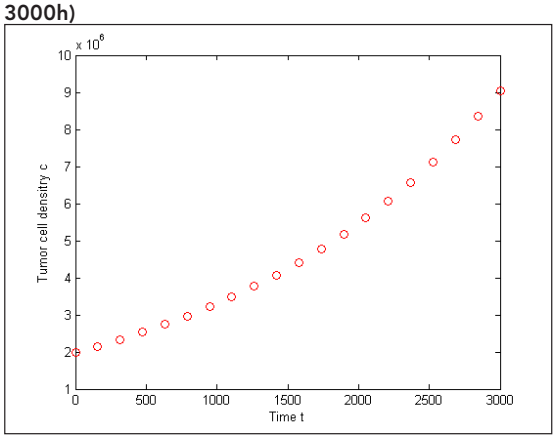
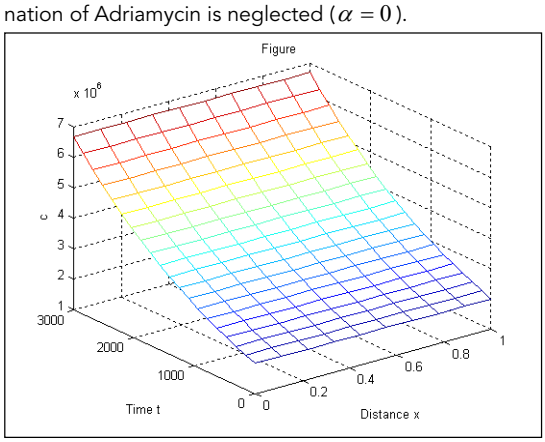


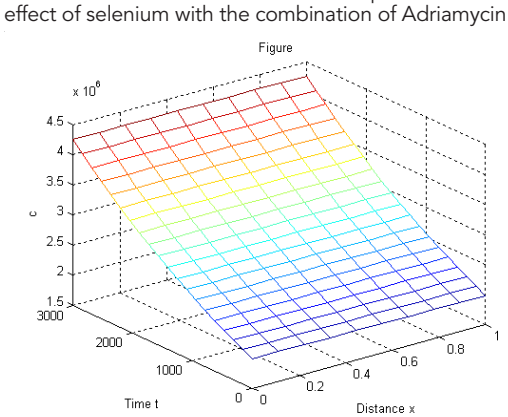
Figure 2: (b) showing the tumor cell density without effect of selenium+adriamycin $\alpha = 0/h$ from the center of the tumor and time (0-3000h)

The figure 2 shows the surface plot tumor cell density with respect to time T and radius x form equation 1.0. I consider the time 0 to 3000 h and radius 0 to 1 mm. I analyzed the growth of tumor cell density in above figure shows the initially, tumor cell density is 1.9×10^{6} cells at initially. After the 3000 h the tumor cell density is almost same at the center and boundary of the tumor, in which the effect of selenium with the combination of Adriamycin is neglected ($\alpha = 0$).



Figures 3: showing the tumor cell density with the effect of selenium+adriamycin $\alpha = 0.0001/h$ distance (0 to 1mm) from the center of the tumor and time (0-3000h).

Figure 3 shows the tumor cell density is cells at initially and after the treatment of 3000h it increases up to cells, in which the effect of selenium with the combination of Adriamycin is /h.



Figures 4: showing the tumor cell density with the effect of selenium+adriamycin $\alpha = 0.00025/h$ distance (0 to 1mm) from the center of the tumor and time (0-3000h).

Figure 4 shows, after the treatment the tumor cell density is 4.2×10^{6} cells, in which the effect of selenium with the combination of Adriamycin is $\alpha = 0.00025/h$.

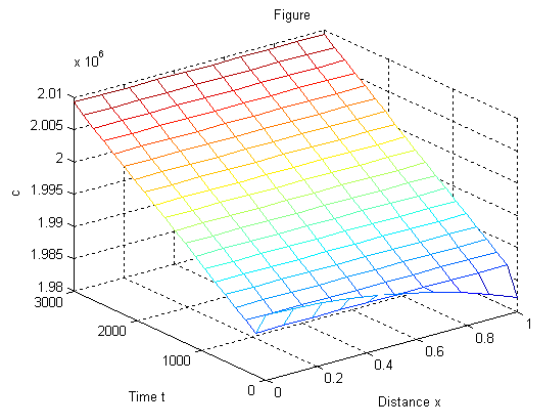
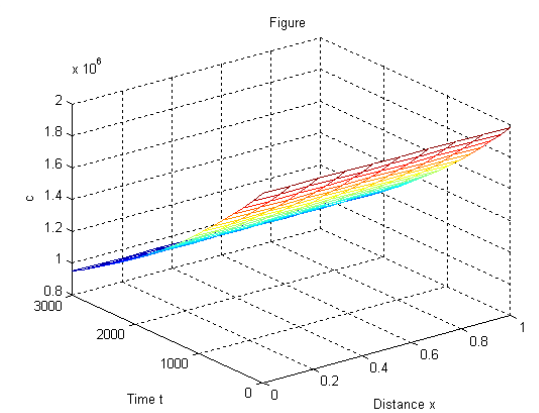


Figure 5 shows, after the treatment the tumor cell density is 2.0×10^{6} cells, in which the effect of selenium with the combination of Adriamycin is $\alpha = 0.0005 \setminus h$.



The figures 6: showing the tumor cell density with the effect of selenium+adriamycin $\alpha = 0.00075$/h distance (0 to 1mm) from the center of the tumor and time (0-3000h).

Figure 6 shows, after the treatment the tumor cell density is 0.9×10^{6} cells, in which the effect of selenium with the combination of Adriamycin is $\alpha = 0.00075/h$. The numerical prediction of our model it possible to compare the mechanisms involved in the appearance of spatio-temporal homogeneities detected in tumor cell culture. It assumes that at initially the tumor cell density is same in different effect of the dose of selenium with the combination of Adriamycin.

Result and discussion.

An enzyme (Adenosine Triphoshate ATP) provides chemical energy for the cell, ATP release energy by releasing a phosphoric acid radical. Then, energy derived from the cellular nutrient causes the acceptor molecule and phosphoric acid to recombine to form new ATP. The entire process continues over and over again. Without that energy, blood vessels cannot grow to the site of a tumor, and without the nutrient supply in blood, tumors cannot grow larger than a pinhead.

The aim to develop a model for studying avascular tumor growth with the effect of dose of the selenium with the combination of Adriamycin. The equations are solved numerically in this case. Throughout the paper, our philosophy when

Volume : 4 | Issue : 2 | Feb 2014 | ISSN - 2249-555X

modeling has been to use the simplest functional forms that capture the physical phenomena. The numerical simulation mainly involved the study of the effects on tumor cell survival of the dimensionless parameter α , which encapsulates the extent of penetration of the chemotherapeutic drug. The simulation emphasize that chemotherapeutic drug penetration is a crucial factor in determining drug effectiveness. The growth of tumor in a spherical shape has been examined in order to describe the initial stages. We have introduced a tumor cell energy model and used tumor cell density with the effect of selenium with the combination of Adriamycin to describe the movement of tumor cells. In section 3 the numerical results suggest that the tumor cell density decreases with the effect of selenium with the combination of Adriamycin. It has been observed for different values of effect of selenium with the combination of Adriamycin. The tumor cell energy decreases with the effect of selenium with the combination of Adriamycin because tumor cell energy fully depends on the tumor cell density.

REFERENCE

1. Martin DS, Stolfi RL, Colofiore JR, Nord LD, Strenberg S.(1994): Biochemical modulation of tumor cell energy in vivo: II. A lower dose of selenium with the combination of Adriamycin is required and a greater antitumor activity is induced when cellular energy is depressed. Cancer Invest. 12(3), 206-307. | 2. RL Stolfi, JR Colofiore, LD Nord, JA Koutcher and DS Martin (1992) Biochemical modulation of tumor cell energy: regression of advanced spontaneous murine breast tumors with a 5-fluorouracil-containing drug combination. Cancer Research, Vol 52, Issue 15, 4074-4081 | 3. Joanna Downer, (2004) "Energy blocker" kills big tumors in rats. jdowner1@jhmi.edu, October 14, Johns Hopkins Medicine, 410-614-5105. | 4. J D Murray (1990) Mathematical Biology. New York: Springer Verlag. | 5. RC Dubey (2004) A text book of Microbiology. Delhi. S. Chand & Company Ltd. | 6. Swanson K R, Bridge C, Murray J D and Alvord E C Jr (2003) Virtual and real brain tumors: using mathematical modeling to quantify glioma growth and invasion. J. Neurological Science 216, | 7. Burgess P K, Kulesa P M, Murray J D and Alvord E C Jr(1997) The interaction of growth rates and diffusion coefficients in a three-dimensional mathematical model of gliomas. J. Neuropath. Exp. Neurol. 56,704. | 8. Miccadei S, Fanciulli M, Bruno T, Paggi MG, Floridi A(1996) Energy metabolism of selenium with the combination of Adriamycin, sensitive and resistant enrich as cites tumor cells. Oncol. Res. 8 (1), 27-35. | 9. JP ward, JR King (1997). Mathematical modeling of avascular tumor growth, IMAJ. Math. Appl. Med. Biol. 14, 39-69. | 10. JP ward, JR King (1999). Mathematical modeling of avascular tumor growth II: modeling growth saturation. IMAJ. Math. Appl. Med. Biol. 16, 171-211. | 11. McDougail SR, Andrson ARA, Chaplain MAj & Sherrat JA (2002). Mathematical modeling of flow Through vascular Netrworks: Implication for Tumor-induceds Angiogenesis and chemotherapy Strategies. Bulletin of Mathematical Biology 64,673-702. | 12. Heidi Fritz, Deborah Kennedy, Dean Fergusson, Rochelle Fernandes, Kieran Cooley, Andrew Seely, Stephen Sagar, Raimond Wong, Dugald Seely mail(2011): Selenium and Lung Cancer: A Systematic Review and Meta Analysis. DOI: 10.1371/journal.pone.0026259, www.ploseone.org. Nov.200