CHAPTER 8

CONCLUSION AND FUTURE RECOMMENDATIONS

8.1 Conclusion

This thesis presented a study of solid tumour growth as explained in Chapter 2 with an emphasis on mathematical modeling. The astonishing theoretical approaches from diffusion model of avasculars tumour to multiphase of vascular tumours including angiogenesis and metastasis are described in detail. Two methods have been applied successfully, that is Adomian Decomposition Method (ADM) and Homotopy Perturbation Method (HPM) to solve these tumour models. Both methods yielded rapidly convergent series solutions for linear and nonlinear problems in the mathematical model. The advantages of these methods are that they provided direct scheme for solving the problem, that is without the need for linearization and discretization. These methods are also eliminated the difficulties and massive computation work found in other numerical computation. Also it is shown that the obtained solution by ADM logically contained the solution obtained by HPM. The benefit of HPM with respect to ADM is that HPM does not involve the Adomian polynomial which is a fundamental qualitative difference in analysis between HPM and ADM.

The first model (Chapter 4) describes the space-time behavior of nutrient concentration diffusing into a spherical tumour with a necrotic core. Both methods showed the similar pattern of nutrient diffusion as the concentration increases with time. The tumour absorbs nutrient quickly when it is placed into high concentration level of nutrient bath. However, the nutrient absorption was affected at different rate of depletion factor. Nevertheless, the tumour still absorb nutrient from its environment and always have more nutrient near the tumour boundary. Our results obtained through this work are more general

than those of Bellomo (2006) since we are taking in account the depletion factor in the equation which Bellomo (2006) failed to do. We also proved the existence and convergence of ADM and HPM solutions through Theorems 4.1 – 4.3. These three theorems are about uniqueness, existence and convergence and have never been proved before.

The second model (Chapter 5) describes the multicell spheroid model which has been extended from the previous model by including a source function S(r) and λ as the inhibitor production rate. The results showed the development of a multicell spheroid from its early stages of growth to its diffusion-limited size of a stable radius of 0.2 cm. It was found that, if the GIF concentration is greater than 1 in any region within the spheroid, then mitosis will be inhibited in that region. This enables regions within the spheroid where mitosis is taking place and where mitosis is inhibited (necrotic core) to be easily distinguished. Our model predicts that the onset of necrosis occurs in the center of the spheroid (C = 1 at r = 0) at a radius between 0.03 and 0.037 cm. The GIF concentration was increased as the time increases. This clearly proves the time dependent of GIF concentration which against Chaplain and Britton (1993) steady-state model. Therefore our model are more general which include the time dependent solution compare to Chaplain and Britton (1993) which simplified the equation into a steady state condition. We also proved the existence and convergence of ADM and HPM solutions through Theorems 5.1 – 5.3.

The third model (Chapter 6) describes the angiogenesis factor in tumour growth. This is an extended model of the previous one with the inclusion of a tumour angiogenesis factor (TAF). We concluded that the initial response of the endothelial cells is essentially one of migration with proliferation of the cells. We also proved that the solution series is convergent from the ratio test. We also proved the existence and convergence of ADM and HPM solutions through Theorems 6.1 – 6.3.

The fourth model (Chapter 7) is related to a tumour invasion and metastasis which includes tumour cells, extra cellular matrix (ECM) and matrix degradation enzyme (MDM). This is an extended model from the previous angiogenesis model. The ECM profile showed clearly the degradation by the MDEs. As the MDEs degraded the ECM, the tumour cells invaded via combination of diffusion and haptotaxis. We also proved that the solution series converged from the ratio test. We also proved the existence and convergence of ADM and HPM solutions through Theorems 7.1 – 7.3.

In conclusion, this work has solved all the four model of tumour growth for the four stages of cancer. To the author knowledge, this is the first work in cancer theoretical research that has successfully obtained the series form solutions for the four stages.

8.2 Future Recommendations

At the present time, the open problems in the study of tumour growth are legion. For instance, an understanding of the phenomenological determinants of cell migration and wheter it is an active or passive process is lacking. Furthermore, the question of the nature of tumour cell migration is central to a number of consequential phenomena such as tumour invasion. The collapse of tumour blood vessels is another poorly understood phenomenon and one which is of fundamental importance to the administration of anti cancer agents. The lacunae in our understanding of tumour growth and invasion necessitate a sustained input by mathematicians into current and future investigations and provide the impetus for a continuing stream of new projects in mathematical oncology and ongoing collaborations between mathematicians and experimentalist. For this reason, the relationship between theory and experiment is a crucial one and one which will guide the progress of cancer research in the future.