CONCLUSIONS

This study used two molecular simulation methods; semi-empirical and *ab initio*. The semi-empirical method has two methods of calculation; AM1 and PM3. The *ab initio* method has also two methods; HF/6-31G and B3LYP/6-31G. The *ab initio* in principle gives the better solution but needs more computational time. The geometry optimization of the doxorubicin and glucosamine(ethylene glycol) molecules can be proposed by AM1, PM3 and HF/6-31G methods. For drug release study, the polymer bond breaking of di glucosamine(ethylene glycol) interacted by acid, normal and base conditions is studied by B3LYP/6-31G//AM1 and B3LYP/6-31G//PM3 methods. The reaction of di glucosamine(ethylene glycol) gives glucosamine(ethylene glycol) which the possibility of micelle formation with doxorubicin (in H-bond study) can be studied by B3LYP/6-31G//PM3 method. The PM3 method can calculate H-bond interaction better than AM1 method in molecular optimization. Beside, the effect of ethylene glycol chain in glucosamine(ethylene glycol) on polymer bond breaking is studied by B3LYP/6-31G//AM1 and B3LYP/6-31G//PM3 methods.

From molecular optimization, the HF/6-31G method can give the optimum structure better than AM1 and PM3 methods. The molecular energy of these optimum structure can be calculated by B3LYP/6-31G method. However, the measurement of bond length, dihedral angle and charge structure by these three methods is not different. Then, these three methods can be used to simulate the molecular structure of doxorubicin and glucosamine(ethylene glycol).

The simulation of drug releasing from capsule polymer is studied by polymer bond breaking of di glucosamine(ethylene glycol) by interacting of H_3O^+ in acid, H_2O in normal and OH^- in base conditions. As a result, the di glucosamine(ethylene glycol) which is a polymer bond can be broken in acid, in normal but not in base conditions. This simulation finds that the acid condition, such as in gastric organelle has possibility to break the capsule polymer bond. Because the ethylene glycol and oxygen molecule have more effect to hydroxide ion in base solution, the electron density in these molecules blocks hydroxide ion to attract the polymer bond. Therefore, this capsule will not be broken in base condition.

The products from polymer bond breaking of di glucosamine(ethylene glycol) which is glucosamine(ethylene glycol) can together with doxorubicin form micelle drug delivery. This micelle formation of doxorubicin and glucosamine(ethylene glycol) depends on length of ethylene glycol chain. This micelle formation, studied from H-bond of the doxorubicin and glucosamine(ethylene glycol) molecules, is calculated by B3LYP/6-31G//PM3 method. The ethylene glycol chain helps doxorubicin and glucosamine(ethylene glycol) on forming micelle structure. If the length of ethylene glycol chain increases, the relative energy of micelle formation decreases. This relative energy decreasing shows that the formation is easier to be formed and more stable. Beside, the molecule of glucosamine(ethylene glycol) variation from 1 to 3 molecules found that the molecule of glucosamine(ethylene glycol) increases, the molecular energy of micelle formation increases, too. Therefore, the glucosamine(ethylene glycol) and doxorubicin can generate the complex molecule in micelle structure to drug delivery system.

According to the micelle simulation, the ethylene glycol chain can help the glucosamine(ethylene glycol) on micelle formation with doxorubicin. Then, the capsule polymer for drug delivery used to carry the doxorubicin should have the suitable length of ethylene glycol chain to help on micelle formation. On the other hands, the ethylene glycol chain might have an effect to polymer bond breaking of capsule polymer. The ethylene glycol chain in glucosamine(ethylene glycol) capsule breaking has been influenced by solution. In acid solution, if length of ethylene glycol chain increases, the bond breaking is easier to occur. Because the ethylene glycol chain can pull the H_3O^+ from solution, the relative energy reduces in transition state step. On the other hand, if the length of ethylene glycol chain is higher, the bond breaking will form with polymer bond. This form (di glucosamine-tri(ethylene glycol)) reacted by H_3O^+ is calculated by PM3 optimization method. In normal and base solutions, the length of ethylene glycol chain increases, the polymer bond is difficult to break. The reason is that the ethylene glycol has steric hindrance with H_2O molecule to attract at oxygen in polymer bond. It also happens in base solution because the ethylene glycol and oxygen atom has steric hindrance with OH^- molecule to attract at polymer bond.

From this study, the di glucosamine-di(ethylene glycol) capsule has many good characteristics to use as the doxorubicin carrier because the ethylene glycol chain gives the significant of micelle formation and protects capsule from moisture.