CHAPTER I
INTRODUCTION

The effective healing of wound that is the appropriate material covering the wound in order to prevent the intrusion of some bacteria into the wound (Kofuji *et al.*, 2010). The wound healing process is a restortarion of injured tissue which consisted of four stages are inflammatory, migratory, proliferative and maturation phase (Zahedi *et al.*, 2009, Sikareepaisan *et al.*, 2011). Addition, the physical forms of wound dressing that present on many difference types like hydrofibres, hydrogels, films, foam dressings, alginates, dressings containing iodine (Watson *et al.*, 2005). Moreover, the material used to produce wound dressing should be biocompatibility, non-toxicity, non-allergenic and non-adherent (Thakur *et al.*, 2008).

The material that has shown property as a constitutive of wound dressing is poly(vinyl alcohol) (PVA), which is a hydrophilic polymer prepared from polymerization of poly(vinyl acetate). PVA is used as a film in many applications of medicine thank to its characteristics such as biocompatibility, nontoxicity, biodegradability, transparent and good film forming (Yang *et al.*, 2004, Batista *et al.*, 2013, Hu *et al.*, 2013).

Previous researches reported that the nanoparticles were used to protect the drugs loaded inside from degradation by heat, light,chemical and controlled the release of drugs into target tissue (Yoksan *et al.*, 2010, Ji *et al.*, 2011). Another material that is interested as a component of wound dressing is chitosan , which is natural polysaccharide obtained by deacetylation of chitin, and it consisted of (1,4)- linked N-acetyl glucosamine and glucosamine. Chitosan and its derivertives have been used in drug delivery for the pharmaceutical and biomedical fields owing to its excellent biocompatibility, nontoxicity, mucoadhesive properties and good drug permeability (Yang *et al.*, 2005, Abdull Rasad *et al.*, 2010, Hosseini *et al.*, 2013). The chitosan application has been limited of its insoluble in water and high pH (PKa ~ 5.5). Therefore, quaternary ammonium chitosan, quaternized derivative of chitosan, was synthesized by introducing quaternary ammonium groups on the NH_2-group of the chitosan backbones for exhibiting excellent water solubility (Sadeghi *et al.*, 2008, Sajomsang *et al.*, 2009, Xu *et al.*, 2011) and ability to itnteract

with other substrat for drugs delivery (Maya *et al.*, 2012). The derivertive is useful for a variety of applications and sutible for a nanoparticles processing (de Britto *et al.*, 2012).

The technique which available for producing quaternary ammonium chitosan nanoparticles is "Inotropic gelation" (Tripathy *et al.*, 2012) using of electrostatic interaction between opposite charged of polycation of chitosan and polyanion of Tripolyphosphte (TPP). In addition, the process is not using organic solvent, nontoxic method and simple method (Keawchaoon *et al.*, 2011). Recently, the loading of bioactives and drugs –such as salicylic acid , gentamicin acid (Ji *et al.*, 2011), ascorbyl palmitate (Yoksan *et al.*, 2010) carvacrol (Keawchaoon *et al.*, 2011) and oregano essential oil (Hosseini *et al.*, 2013) into chitosan nanoparticles via inotropic gelation had been reported. (Janes *et al.*, 2001) revealed that the loading of doxorubicin into chitosan nanoparticles could extend the release of doxorubicin and (Maya *et al.*, 2012) revealed that the loading of teracycline into O-carboxymethyl chitosan nanoparticles could against the infections of Staphylococcus aureus and non-toxic with NIH-3T3, L929, HEK-293 epithelial cell lines and THP-1 monocytic cells.

The present research thus focuses on the synthesis of quaternary ammonium chitosan by chemical modification and preparation of material by using PVA film containing quaternary ammonium chitosan loaded tetracycline nanoparticles *via* a solution casting method. Tetracycline (TC) was chosen as a antibiotic drug because it has high efficacy against both of gram positive and gram negative bacteria (Chopra *et al.*, 2001). The nanoparticles were characterized by UV-Vis spectrophotometry, Fourier transforminfrared spectroscopy (FT-IR), scanning electron microscope (SEM), dynamic light scattering (DLS), X-ray diffractometer (XRD) and Zeta potential measurement. The effects of initial tetracycline content on encapsulation efficiency (EE), shape , size were also investigated. The antibacterial activities of wound dressing were studied againts *Escherichia coli*, *Enterococcus faecium*, and *Staphylococcus aureus* by disk diffusion method (AATCC 147) and broth dilution method. Finally, the indirect cytotoxicity of the wound dressings was studied in mouse fibroblast (L929) and human fibroblast cells by using MTT assay.

In addition, The drug release kinetic was studied in acetate buffer solutions pH 5.5 and in phosphate buffer solutions pH 7.4.