SUMMARY
Toxoplasma gondii is a cosmopolitan parasite that can live in most climates all over the world. It is one of the major pathogenic intracellular protozoan probably infect all warmblooded animals. Toxoplasmosis causes potential risk to human and major economic losses in all classes of livestock, because it considered as the causative agent of a zoonotic disease. Infection or reactivation of chronic infected immunodepressed patients and people with organ transplantation, leads to life-threatening toxoplasmic encephalitis and increase mortality rate. T. gondii cause congenital disease and may be ending by death to the intermediate hosts neonatal loss in human and animals. Previous studies indicate the high prevalence of toxoplasmosis in Egypt in human, turkeys, chickens, ducks, Donkeys, camels and equine. RH is virulent T. gondii strain led to acute toxoplasmosis by invading and rapidly undergoes unlimited proliferation in all nucleated cells of warm blood animals ending with mice death. T. gondii is polyxenous parasite and the avirulent strain form tissue cyst. It has facultative heteroxenous complex life cycle that contain four infectious stages; the tachyzoite, bradyzoite, merozoite and sporozoite. The sexual stage occurs only in felines producing up to millions of unsporulated oocysts which expelled with stool after prepatent period, later the unsporulated oocysts transformed into infective sporulated oocysts after few days. Oocyst is an important stage in transmission where it contaminates the rural environment. T. gondii can enter bodies through conjunctiva, nasal, pharyngeal, respiratory, and percutaneous. The major is the hygienic routes such as ingestion of fresh, or under cooked meat, drinking water, fluids as well as unwashed vegetables. Also, the fur of dogs and cats, acts as a mechanical carriers because dogs had a habit of seeking out and rolling in cat feces. Trans-placental transmission may occur in human and other intermediate hosts. In addition, organ or stem cell transplantation transmits the infection if the donor was infected. The clinical symptom ranges from no noticeable symptoms to a syndrome of fever and lymph adenopathy to diffuse multi-system organ. Sulfonamides, clindamycin and other chemicals are
used for treatment of toxoplasmosis, such drugs had many toxic effects and re-infection may occur. A commercial vaccine was developed but, it was not widely used as a consequence of reactivation of parasite to the pathogenic form, short shelf life, and high cost. Under this scenario, development of new vaccine is an attractive goal. The aim of the present study is to highlight and studying the different histopathological and histochemical changes that resulted after challenging the vaccinated murine models with the highly virulent RH *T. gondii* tachyzoite. Also, the immune responses of mice that may be associated with the protective capacity of the ultraviolet-exposed parasite will be investigated. In addition, this study is a trial to explore the feasibility of developing a cheap vaccine against *T. gondii* parasitic infection, where UV-light is cheap and safe. Moreover, this might be useful in the protection of economically important live stock. As a first step towards the identification of a subunit vaccine candidate the ultravioletattenuated or -killed parasite, murine model will be used. Different techniques were used to monitor the consequence of this goal protective capacity by measuring different parameters like: ¹- histopathological pictures by Haematoxylin & Eosin. ²- histochemical profile: Feulgen’s method for DNA detection and Periodic acid Schiff’s technique for polysaccharides demonstration. ³- The immunological response in mice was monitored by measuring IL-¹, IFN-γ production and splenocytes proliferation from stimulated culture splenocytes. ⁴- The survival rate was recorded. The present study showed that *T. gondii* RH strain caused many histopathological alterations in liver and brain tissues, represented by pyknosis, necrosis, cell death, vacuolations, dilatation of blood vessels, vasculitis, leukocytic infiltrations, gliosis, thickening of hepatic capsule and meningitis. Histochemical changes demonstrated as exhausting of the polysaccharides contents, losing considerable amount of protein materials and decreasing the DNA from infected cells and the surrounding tissues. The previous events lead to loss of appetite, ruffling of hair sudden organ failure, like liver and finally death of the animal. The innate immune response could not control the highly replicated tachyzoites; moreover it led to tissue destruction by uncontrolled production of inflammatory cytokines. The
mortality of mice in this group reaches to ١٠٠٪. KSU T. gondii cystogenic strain little histological and histochemical changes occur where the parasite is nonvirulent and the immune system easy control it. The tachyzoite transformed to latent dormant stage called tissue cyst that consists of bradyzoites and surrounded by parasitophorous vacuole. The bradyzoites enriched with protein content and contain remarkable amount of polysaccharides moreover, the Feulgen reaction reflect high DNA content.

In this study RHT were attenuated by exposing to UVirradiation with ٩٤٫٢ mw-min/cm² (ARHT) and ٣٫٣ mwmin/cm² (KRHT), then mice vaccinated either with ARHT or KRHT at the beginning of experiment and a booster dose was given at ١٤٠ DP ١٨٠. Later the vaccinated mice were challenged with RHT at ١٠٠ DP ١٦٠٠. These trials as a vaccine gave good results represented by gradual enhancement of histopathological picture of tissue destruction and finally recover of animal. Also, the histochemical profile greatly improved as noticed by increasing different histochemical material like polysaccharides, protein and DNA, which reached to level approximately equal to the normal control mice.

The survival rates remarkably increased up to ١٠٠٪ and to ٨٠٪ in KRHT and ARHT in vaccinated challenged mice. The successfulness of immune responses in vaccinated challenged mice was obvious in formation of protective capacity that represented by parasite elimination or at least forcing tachyzoites to transform into ill formed tissue cyst. Moreover, a regulated secretion of IL-١ and INF- level was recorded, and there was increase in splenocytes proliferation in response to STAg stimulation denoting to the formation of memory cells which are important in the protective immunity.

It is worthily to mention that the protective capacity was persisted for ٩ months after vaccination, and mice during this time point was continued to overcome a second lethal challenge with ١٠٠ RHT. More over, the mice offspring were survive healthy (unpublished result of the same study). The present results of histological, histochemical, survival rates and immunological studies may reflect gradual buildup of solid immunity against re-infection with T. gondii.