Herbal medicine has been recently recognized as a type of the alternative medicine and become widely spread as a back look trial to the natural means of treating many diseases, however using medicinal herbs and plants is not less exposed to risks. as many of these plants, used in herbal medicine, are extremely toxic. Peganum harmala, for instance, is one of these plants which is widely used in the herbal medicinal in the treatment of several diseases in many countries including Saudi Arabia. The current study was aimed to investigate the effects that might be resulted from the administration of Peganum harmala seeds on some physiological, histological, and behavioural aspects. The effects of chronic administration of two doses of the aqueous extract of Peganum harmala seeds [on male and female "MF1" albino mice] were studied. The blood biochemical results of the liver and kidneys physiological functions tests showed that chronic administration of 200mg/kg dose (i.p. and p.o.) for six weeks induced highly significant increase in the levels of liver enzymes such as: SGPT, SGOT, and Alkaline Phosphatase, it also caused a significant increase in the levels of : Creatinine, Blood Urea and Uric Acid. These results reflect the extreme toxicity of Peganum harmala seeds as it induced severe defects in the physiological functions of the liver and kidneys. This physiological defect was accompanied with severe histopathological damages in these organs in the form of: acute hepatic inflammation, Hepatocytes swelling as a result of lipid accumulation which may indicate the occurrence of fatty degeneration, extreme laceration of the hepatic lobules structure. On other hand the chronic administration of dose 200mg/kg induced severe histological damages in the kidneys in the form of: Glomerular atrophy, and degeneration of the distal convoluted tubules. On other aspect, the neurophysiological results showed that chronic administration of 200mg/kg dose induced significant increase in the levels of Dopamine, Serotonin, Epinephrine and Norepinephrine in the seven different brain areas. These neurophysiological results aproved that Peganum harmal seeds contained neuroactive compounds. The above treatment also produced inhibition in the aggressive behaviour and in the locomotory behaviour ( represented by a significant decrease in number of squares crossed by animals, and a significant increase in the immobility period). In addition the chronic administration of 200mg/kg dose of Peganum harmala seeds extract during pregnancy induced severe toxic effects on pregnant females mice, fetuses and newborns. The present results showed that administration of the above dose during pregnancy period caused abortion in the pregnant treated mice, and accompanied by fetuses degeneration inside mothers uterus, and a significant increase in the percentage of dead pups. All these negative effects of Peganum harmala seeds assured and proved the toxicity of these seeds and the dangers of using it for long duration, specially during pregnancy and lactation period. Therefore at the end of the current study we recommend that patients should be very cautious while using the seeds of Peganum harmala (for any therapeutic purposes through herbal medicine) due to its extreme toxicity. Further clinical studies are recommended to examine the effects of these seeds on human subjects to investigate any possible negative effects on the patients health.