Abstract Structural modifications in polymers have been of great commercial and scientific interest in obtaining new materials. Such modifications can be obtained in the presence of a cross-linking agent or gamma irradiation, physical process, among others, forming three-dimensional networks. These networks are responsible for the insolubility and stability of these hydrogels. The balance between the dispersion forces acting on the hydrated chains and the cohesive forces due to the covalent cross-links causes or does not cause the swelling ability. Other characteristic interactions are also present, including electrostatic and dipole-dipole interactions, characterizing the degree and nature of the cross-links responsible for their characteristics in the swollen state. The objective of this study was to develop poly (vinyl alcohol) (PVA) hydrogels with and without papain, by freezing and thawing, and PVA hydrogels irradiated at 25 kGy, in order to compare the swelling behavior between the two techniques. Characterizations were used: swelling, infrared spectrometer with Fourier transform (FTIR), in vitro release. The results indicate that increased thermal cycling reduces swelling. This reduction was associated with increased crystal reticulum, however increased reticulum did not significantly affect the release of papain. The results are satisfactory as expected, allowing the development of the project in order to obtain matrices for future applications.