In the current article, an experimental investigation has been implemented of flow and heat transfer characteristics in a parabolic trough solar collector (PTSC) using both nano-fluids and artificial neural networks modeling. Water was used as a standard working fluid in order to compare with two different types of nano-fluid namely, nano-CuO /H2O and nano-TiO2/ H2O, both with a volume concentration of 0.02. The performance of the PTSC system was eval-uated using three main indicators: outlet water temperature, useful energy and thermal efficiency under the influence of mass flowrate ranging from 30 to 80 Lt/hr. In parallel, an artificial neural network (ANN) has been proposed to predict the thermal efficiency of PTSC depending on the experimental re-sults. An Artificial Neural Network (ANN) model consists of four inputs, one output parameter and two hidden layers, two neural network models (4-2-2-1) and (4-9-9-1) were built. The experimental results show that CuO/ H2O and TiO2/H2O have higher thermal performance than water. Overall, it was veri-fied that the maximum increase in thermal efficiency of TiO2/H2O and CuO/H2O compared to water was 7.12% and 19.2%, respectively. On the oth-er hand, the results of the model 4-9-9-1 of ANN provide a higher reliability and accuracy for predicting the Thermal efficiency than the model 4-2-2-1. The results revealed that the agreement in the thermal efficiency between the ANN analysis and the experimental results about of 91% and RMSE 3.951 for 4-9-9-1 and 86% and RMSE 5.278 for 4-2-21.