This study focuses on botanical features gleaned from the literary source *Hypnerotomachia Poliphili* (1499); the analysis reveals that *Hypnerotomachia Poliphili* includes 285 botanical entities associated with 672 textual passages, which have not hitherto been reported. Roses, myrtle, pines, cypresses, laurel, acanthus, oaks, junipers, ivy, thyme, violets, sandalwoods and orange trees are the most frequently cited plants. Shrubs dominate with 43%, while herbs and trees follow with 28% and 26%, respectively. Arbutus, dittany, cypress, fig tree, labdanum, laurel, myrtle, oaks, oleander, wild and cultivated olive trees, oregano, pine, thyme, grapevines are associated with the diversity of Mediterranean ecosystems. In addition, numerous textual passages of *Hypnerotomachia Poliphili* mentioning flowering and fruiting plants reveal the seasonality of the Mediterranean region. Exotic plants, such as frankincense tree, myrrh, banana, pepper, sandalwood and jasmines are also included. Thorny plants, sharp thistles and cedars are cited in the text as occurring among ancient monuments and historical ruins. The botanical content of *Hypnerotomachia Poliphili* constitutes an alternate source of botanical observation, which includes historical, allegoric and symbolic information.