We recently proposed a novel single-source integral equation (SSIE) for accurate broadband resistance and inductance extraction and current flow modeling in 2-D conductors. The new surface integral equation is advantageous compared with the traditional volume electric field integral equation (V-EFIE) used for the inductance extraction, since the unknown function is defined on the surface of conductors as opposed to the volumetric unknown current density in V-EFIE. The new SSIE is also more suitable for the solution of inductance extraction problems than the traditional surface integral equation formulations, as it features only a single unknown surface function as opposed to having the unknown equivalent electric and magnetic surface current densities. The new equation also features only the electric field Green's functions unlike the previously known SSIE formulations. The latter property makes the new SSIE equation particularly suitable to the inclusion of the multilayered substrate effect into the inductance extraction model. This paper describes the generalization of the new SSIE formulation to the case of transmission line models embedded into the multilayered lossy substrates. This paper also shows how the matrix sparsity in the method of moments discretization of the novel integral equation can be exploited to accelerate its numerical solution and reduce associated memory use. This sparsity arises due to the skin-effect-based attenuation of the fields in conductors' cross sections leading to vanishing levels of the matrix elements corresponding to the distant interactions. Typical examples of inductance extraction in complex interconnects situated in lossy substrate are considered to validate the proposed techniques against traditional approaches.