Quinine (an antimalarial drug) and aspirin, a nonsteroidal anti-inflammatory drug (NSAID) with antipyretic, anti-inflammatory, and analgesic use, were combined into a new drug–drug salt, quininium aspirinate, by neat milling in a ball mill (or an agate mortar) and liquid-assisted grinding using stoichiometric amounts of the reactants in a 1:1 molar ratio, and water, EtOH, toluene, or heptane as additives. A tetrahydrofuran solution of the mechanochemical product prepared using EtOH as an additive led to a single crystal of the same material obtained by mechanochemistry, which was used for crystal structure determination at 100 K. Powder X-ray diffraction ruled out crystallographic phase transitions in the 100–295 K interval, and it was used to calculate the unit cell parameters at ambient temperature. Neat mechanical treatment (in a mortar and pestle, or in a ball mill at 20 or 30 Hz milling frequencies) gave rise to an amorphous phase, as shown by powder X-ray diffraction. However, FT–IR spectroscopy data unambiguously shows that a mechanochemical reaction has occurred, since an intense and non-overlapped band of aspirin is absent in the mechanochemical products by neat ball milling or neat grinding. Milling the reactants without liquid additives at 10 and 15 Hz milling frequency for the same time period led to incomplete reactions, due to the mechanical energy provided to the reactants did not afford the completion of the reactions. Thermogravimetry and differential scanning calorimetry indicated that the amorphous and crystalline mechanochemical products form glasses before melting, and they do not recrystallize upon cooling. The amorphous material obtained by neat grinding or milling crystallizes upon storage (in the order of two years) into the salt which crystal structure is reported. The measured aqueous solubility of quininium aspirinate is 3.8 mg/mL, larger than the solubility of the marketed quininium sulfate (1.20 mg/mL). This makes quininium aspirinate a potentially useful new drug-drug combination for the prevention or the treatment of malaria fevers, due to aspirin is an antipyretic and it is used for the prevention of heart disease. The mechanochemical synthesis, crystal structure analysis, Hirshfeld surfaces, powder X-ray diffraction, thermogravimetry, differential scanning calorimetry, and FT–IR spectroscopy data of quininium aspirinate will be reported.