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索拉非尼固体脂质纳米粒冻干粉制备及体外释药特性研究

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- 摘要
- 参考文献
- 相关文章

摘要 目的 制备索拉非尼固体脂质纳米粒，并考察其理化性质及体外释药特性。方法 采用乳化蒸发-低温固化法制备索拉非尼固体脂质纳米粒，透射电镜观察形态，激光粒度仪测定粒径和Zeta电位，葡聚糖凝胶法和HPLC测定其包封率，透析法考察其体外释药特性，冷冻干燥法制备索拉非尼固体脂质纳米粒冻干粉，差示扫描量热分析其物相状态。结果 制得索拉非尼固体脂质纳米粒为类球形实体，粒径分布比较均匀，平均粒径为(108.2±7.0) nm，多分散指数为（0.250±0.022），Zeta电位为(-16.4±0.7) mV；测得3批样品的平均包封率为(73.49±1.87)%；体外释放符合Weibull模型；等体积15%甘露醇作冻干保护剂效果较好；DSC分析证明纳米粒已形成。结论 乳化蒸发-低温固化法适用于索拉非尼固体脂质纳米粒的制备，所制纳米粒各项物理指标稳定，具有明显缓释作用。

关键词： 索拉非尼 冻干粉 固体脂质纳米粒 乳化蒸发-低温固化法 物相分析 体外释放

Abstract： OBJECTIVE To prepare sorafenib solid lipid nanoparticles and investigate its physicochemical properties and *in vitro* release profile. METHODS Sorafenib solid lipid nanoparticles were prepared by emulsion evaporation-solidification at low temperature. The morphology was examined by transmission electron microscope. The particle size and Zeta potential were determined by laser granularity equipment. The encapsulation efficiency was detected by Sephadex gel chromatography and HPLC. The *in vitro* release profile of sorafenib solid lipid nanoparticles was studied using dialysis technology. The lyophilized powder of sorafenib solid lipid nanoparticles was prepared by refrigerated air dryer and its material phase was analyzed by DSC. RESULTS The sorafenib solid lipid nanoparticles assumed spherical shape. The distribution of diameter was even with average particle size of (108.2±7.0) nm. The PDI and Zeta potential were （0.250±0.022） and (-16.4±0.7) mV，respectively. The average encapsulation efficiency was (73.49±1.87)%. The release *in vitro* accorded with Weibull order model. Equal volume of 15% mannitol was the best protective agent for lyophilized powder of sorafenib solid lipid nanoparticles. The formation of a new material phase was testified by analysis of DSC. CONCLUSION The method of emulsion evaporation-solidification at low temperature was appropriate for preparation of sorafenib solid lipid nanoparticles. The nanoparticles had stable physical properties and significant sustained-release effect.

Keywords： sorafenib, lyophilized powder, solid lipid nanoparticle, emulsion evaporation-solidification, material phase analysis, *in vitro* release

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