

聚左乳酸(PLLA)之生物相容性研究

The study of PLLA biocompatibility

中文摘要

聚左乳酸(PLLA)的應用相當廣泛，從以前工業用的罐子，不織布，至今已發展應用到生物醫學方面，如縫線，牙周再生膜，手術骨釘骨板等等。PLLA 分子量越高，機械強度越強，因此適合用於手術固定用之骨釘骨板的固定，但缺點是在人體內的降解時間就越久；而較低分子量的 PLLA，雖然降解較快，卻因為機械強度較差的關係，則多使用在受力較小的部位。本實驗室與某生技公司所合力開發出具商業化潛力的低分子量(140-160KD)PLLA 試片，擁有與高分子量 PLLA 相當的機械強度。爲了了解本 PLLA 試片在活體內降解的過程中是否會引起某些層面的生物反應，本實驗將對 PLLA 試片以及其降解產物對生物細胞、過敏反應以及基因突變的影響來做相關的探討。爲了模擬材料在活體內的環境，本研究欲檢測 PLLA 萃取液、降解產物，以及 PLLA 試片對 3T3 fibroblast 是否具有細胞毒性。植入體內的 PLLA，細胞必須要先能附著在其表面上，進行增生，進一步分化而行使正常功能。因此，本實驗也探討細胞對 PLLA 試片的附著與增生能力，以 polystyrene culture disc 作爲控制組，另外並以接觸角測定儀與表面粗糙度儀來測量 PLLA 試片與 polystyrene culture disc 的親水性與表面粗糙度。敏感性測試與基因毒性測試則分別是以天竺鼠與特定的沙門氏菌來研究試片的致敏性與致突變性。實驗結果顯示，即使是最高濃度的 PLLA 萃取液與降解產物，均不會產生任何的細胞毒性、基因毒性與致敏性。PLLA 試片表面與水的接觸角以及的粗糙度分別爲 70°與 0.51 μm ，而控制組 polystyrene culture disc 則爲 50°與 0.28 μm 。細胞在 PLLA 試片上的附著能力略優於控制組(p<0.05)，附著率從加入細胞後 12 小時以前的 2.5x10² / hr，增加到 12 小時以後 2x10³ / hr，而兩者的增生能力則是無統計上之差異。本實驗所採用的 PLLA 試片具有不錯的生物相容性，未來應用在各種不同的醫療用途是深具潛力的。

英文摘要

Since PLLA (poly-L-lactic acid) was produced by heating lactic acid under vacuum in 1932, it has been used in biology and medicine. PLLA possesses many desirable properties that make it advantageous for many medical applications, such as sutures, surgical bone plates, GTR membranes, etc. The aim of this study was to evaluate the short-term biocompatibility of a low-molecular-weight (140-160KD) PLLA disc which has a good mechanical strength. The effects of 1-, 3-, 5-day PLLA extracts and its artificial degradation products obtained by heating at 90°C for 30hrs on 3T3 fibroblast were studied by MTT assay. The abilities of the PLLA disc surface to allow

cell attachment and subsequent proliferation were also evaluated. In addition, the surface roughness and wettability were examined by mechanical surface profilometer and contact angle meter, respectively. The abilities of PLLA extracts and degradation products to cause allergic reaction on guinea pigs were detected by sensitization test (Buehler test), and their mutagenic potential were performed by Ames test using *Salmonella typhimurium* as test strains. The PLLA disc, PLLA extracts and degradation products did not show cytotoxic, allergic, or genotoxic activities. The PLLA surface roughness and the contact angle measured were $0.51 \mu\text{m}$ and 70°C , and the polystyrene culture disc were $0.28 \mu\text{m}$ and 50°C . The surface roughness of PLLA disc seemed to facilitate cell attachment, but the subsequent proliferation has no difference as compared to the polystyrene culture disc. These results suggest the low-molecular-weight PLLA used in this study may be regarded as a promising biomedical material.