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論文内容の要旨

Recent demands for low-temperature sterilization in the medical and food industrial fields have prompted the development of various novel sterilization techniques, such as plasma sterilization and electron beam sterilization among others. Until now, dry heat or hot steam techniques such as the autoclave, ethylene oxide (EtO) gas sterilization and gamma-ray sterilization have mainly been used in sterilizing medical instruments. Dry heat or hot steam sterilization can be applied only to objects that can withstand high temperatures. In contrast, EtO gas sterilization can be used on heat-sensitive materials, but the EtO gas itself is toxic, carcinogenic and inflammable and poses a threat to the environment in the form of chlorofluorocarbons. Gamma-ray sterilization techniques can be used on medical instruments after covering them with plastic sheets or carton cases. However, this technique is expensive and there is a concern that the materials may be modified physically by the gamma-ray irradiation.

A recent development has been the application of plasma discharge to sterilization. Plasma sterilization methods have several advantages over conventional methods, including a low sterilization temperature (typically less than 70℃) and a short sterilization period of several minutes to one hour. By using higher microwave power, we can achieve the same sterilization in a shorter treatment time. However, the risk of heat damage caused by the surface contact between the plasma and the medical instrument becomes serious, especially for plastic materials. For this study, to achieve sterilization at a low temperature of less than 70℃, a pulse-modulated microwave system was used. The sterilization characteristics of 10^6 G. stearothermophilus spores as biological indicator (BI) were studied. Mechanisms of plasma sterilization were studied in O_2, N_2 and N_2-O_2 plasmas. To expand the application of microwave plasma sterilization technique, a large-volume medical sterilizer using microwave plasma, which could achieve large sterilization volume and internal sterilization effect, was developed.

For plasma sterilization, the BIs used were G. stearothermophilus spores with population of 10^6, which were spread on a small stainless steel disc and placed in Petri dishes set on a movable substrate stage about 15-23 cm below the quartz vacuum window in 40-cm-diameter surface-wave plasma (SWP) device. During plasma irradiation, the stage temperature was measured using thermo-label sheets attached to the Petri dish. After plasma irradiation, the spores were incubated in culture solution for seven days at an incubation temperature of 55-60℃. Subsequently, it could be determined whether the spores had been killed or not because the colour of the culture solution changed from purple to yellow if the spores were still viable.

Sterilization of BI samples with 10^6 G. stearothermophilus spores was confirmed using continuous wave (CW) SWP in O_2, N_2 and N_2-O_2 mixture gas within 4 min. It was found that all the BI samples were sterilized by the pulse-modulated oxygen plasma when the total microwave on time was longer than 120 s, even when the on-duration per pulse was 10μs. Based on the thermo-label measurements, it can be shown that the surface temperature of the Petri dish during total processing period, was always less than 70 ℃. When the total microwave on time was much shorter than 120 s, we found that a longer on-duration per pulse was required for successful sterilization.
To study the mechanism of plasma sterilization, diagnoses of plasma using optical emission and mass spectrometry, and SEM analyses of shapes of spores after plasma treatments were applied. There exist UV emissions in N_2-O_2 mixture gas discharge plasma. Several strong lines at 282.0, 297.7, 313.6, 315.9, 337.1, 357.7 nm were originated from the second positive systems ($C^3\Pi_u \rightarrow B^3\Pi_g$) of N_2 molecules. Several UV emissions at 214.1, 226.9, 237.0, 247.9, 258.8 nm were considered originated from NO γ system ($A^2\Sigma+ \rightarrow X^2\Pi$). They might play some role in sterilizing the spores in addition to N_2 positive system in the wavelength region of 300～400 nm and the etching process due to oxygen radicals.

In the new large-volume microwave plasma sterilizer, a discharge transition between SWP and volume-wave plasma (VWP) could be controlled. So far, we have demonstrated sterilization of the spores packaged in glassine pouch using SWP/VWP filled the new sterilizer with air-simulated N_2-O_2 gas mixture. We have confirmed that the wrapped 10^8 Bacillus atrophaeus spores and 10^7 G. stearothermophilus spores were sterilized by CW or time-modulated microwave excited O_2, N_2 and N_2-O_2 plasmas for net on time of roughly 20 min. When water vapor was added on different gas species plasma, it has been found a great improvement on sterilization effect, especially on internal sterilization of polyethylene (PE) film wrapped materials.

The possible sterilization mechanisms were studied and summarized as presented below. When microwave energy was induced to a chamber filled with oxygen, nitrogen and pure water, microwave plasma was excited, then UV radiation, oxygen radicals and some strong oxidizer would be produced. Consequently, spores will be inactivated by UV radiation, be etched by oxygen radicals, be oxidized by some strong oxidizer. If spores were wrapped by PE film, oxygen radicals would loose energy while contacting PE film, therefore, oxygen radicals would be shut down by PE film.

論 文 審 査 結 果 の 要 旨

近年、医療用滅菌としてエチレンオキサイドガス滅菌あるいは高圧蒸気滅菌（オートクレーブ）が広く用いられている。しかしながら、前者では低温処理は可能であるが、ガスの毒性など環境面の問題が指摘されており、後者では121℃での高温処理のため耐熱性の材料に限定されるなどの問題が残されている。またγ線や電子線を用いる滅菌法では、大型設備が必要であるなど、コスト面の問題や滅菌対象物の改質の問題が指摘されている。このような背景の下、近年、プラズマを用いた低温滅菌法が注目されている。本論文は、低圧力マイクロ波放電プラズマおよび大気圧放電プラズマを用いた有害物質を用いない低温プラズマ滅菌に関する実験結果をまとめたものである。

第1章は序論で、従来用いられている種々の滅菌・殺菌法を紹介し、プラズマ滅菌に関する研究動向および本論文の位置づけを述べている。第2章では滅菌実験に用いたマイクロ波励起表面波プラズマの生成装置および放電特性について記述している。また第3章では表面波プラズマと体積波プラズマの放電特性の違いを述べ、大容積マイクロ波プラズマ実験装置を用いた実験により、両者放電プラズマ間の遷移を入射パワーと動作圧力により容易に制御できることを示している。第4章は、本研究で用いた滅菌評価法について記述している。第5章では、表面波プラズマによる低温滅菌実験の結果を示し、酸素プラズマでは酸素ラジカルによるエッチング効果が、窒素プラズマでは波長帯域280nm ～ 360 nmにおける窒素分子からの紫外線発光が主な滅菌要因であることを示している。また、空気を模擬した窒素・酸素混合ガスを用いたプラズマでは、上記の効果に加え、波長帯域200 nm ～ 280 nmにおける一酸化窒素からの紫外線発光が相乗的に作用し、さらに高速な滅菌特性が得られることを明らかにしている。第6章では包装された医療器具の滅菌を実現する方法として体積波プラズマを用いた低温滅菌法を提案し、温度90℃程度において10^4～10^8個の枯草菌を約20分間で死滅できることを示している。なお、さらに低温化を実現するため、パルス放電プラズマを用いた滅菌実験を実施し、水蒸気を添加した空気模擬プラズマにおいて温度60℃以下で10^6個の枯草菌の死滅を確認している。第7章では大気圧アルゴンプラズマジェットを用いた滅菌実験について記述し、その滅菌要因が大気中で生成されるオゾンおよび窒素分子から放射される紫外線発光の可能性があることを示している。第8章はまとめであり、本論文の結果を総括している。

以上のように、本研究では低圧力マイクロ波放電プラズマおよび大気圧放電プラズマを用いた低温滅菌の可能性を示し、今後の医療分野あるいは食品分野への応用に関する有用な知見を与えている。よって、本論文は博士（工学）の学位を授与するに充分な内容であると認定する。