doi:10.4172/0975-0851.1000007

TITLE

IN-VITRO AND IN-VIVO EVALUATION OF MICROPROCESSOR CONTROLLED IONTOPHORETIC TRANSDERMAL DRUG DELIVERY OF ANTI-CANCER DRUGS

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Microprocessor controlled Iontophoretic transdermal delivery of anticancer drugs 5-Fluorouracil (5-FU) and 6-Mercaptopurine (6-MP) was developed and in-vitro evaluation and bioavailability studies was done. The patches were evaluated physiochemical properties and In-vitro permeation studies through human cadaver skin showed, passive delivery (0.0mA/cm^2) of 6-MP was low. As the current density was progressively increased, the flux also increased. the flux also increased with 0.1 mA/cm^2 for 15-20 minutes, but it was less than desired flux, 0.2 mA/cm^2 for 30 minutes showed better flux than 0.1mA/cm^2 current, but lag time was more than 4 hours, 0.5mA/cm^2 current for more than 1hour, flux was > 159g/cm2 h which was desired flux for 6-MP. 5-FU flux reached the MEC (minimum effective concentration) of 54 µg/cm2 h with 0.5 mA/cm2 current for 30-45 minutes, drug concentration were within the therapeutic window in post current phase. We concluded from Ohm's Law as the resistance decreases, current increases. Interestingly, for all investigated current densities, as soon as the current was switched off, 5-FU and 6-MP flux decreased fairly, but the controlled drug delivery was achieved by switching the current for particular period of time. Pharmacokinetic studies in rabbits for 0.25mA/cm2 for 30 min in 6-Mercaptopurine patches Tmax (min) 45 ± 13.2, Cmax (ng/ml) 194.6± 47 , t1/2 (min) 225 ±16.8, AUC0-∞ (ng/ml/h) 340.18±16, AUC0-t (ng/ml/h) 299.14±43 and 0.5mA/cm2 for 30 min in 5-Fluorouacil patches Tmax (min) 30 ± 6.3, Cmax (ng/ml) 863.25 ± 32, t1/2 (min), 95 ± 0.5, AUC0-∞ (ng/ml/h) 1567± 36, AUC0-t (ng/ml/h) 1198.76± 24. The Pharmacokinetic studies carried out in rabbits resulted in a plasma concentration profile in the therapeutic range. The elimination half-life of drugs was prolonged to very significant extent compared to conventional route of administration oral and intravenous.