The purpose of this research work was to develop and evaluate matrix-type, drug reservoir type, bilayer Membrane Moderated type of Transdermal drug delivery system containing Indomethacin, piroxicam and ondansetron HCL drugs with different ratios of hydrophilic and hydrophobic polymeric combinations by the solvent evaporation and solvent casting technique. The physicochemical compatibility of the drugs and the polymers were studied by FTIR. The results suggested no physicochemical incompatibility between the drugs and the polymers. All this Transdermal patch formulations consists of hydroxy propyl methyl cellulose E5, E15, Eudragit L100, PVP K30, Eudragit RLPO and Ethyl cellulose in the different ratios respectively were prepared. All formulations carried penetration enhancer and plasticizer in chloroform, dichloromethane and methanol as solvent system. All The prepared Transdermal patches were evaluated for moisture absorption, moisture loss and mechanical properties. The diffusion studies were performed by using Franz diffusion cells. The entire formulations of batch F8, F6 and F6 with combination of polymers showed maximum release in 24 h in controlled manner. Hence, it can be practically concluded that Indomethacin, Piroxicam and ondansetron HCL can be formulated into the Transdermal matrix type, drug reservoir type; bilayer Membrane Moderated type patches to sustain its release characteristics.