REVIEW OF CLINICAL PHARMACOLOGY AND
PHARMACOKINETICS, INTERNATIONAL
EDITION 20: 263 (2006)
©PHARMAKON-Press

Pharmacological Profile of DPG-4 a new Ligand for CB1 and CB2 Cannabinoid Receptors

George Panagis[1], Katerina Antoniou[2], Kyriaki Thermos[3], Maria Papazoglou[3], Niki Mastrodimou[3], Alexia Polissidis[4], Styliani Vlachou[1], Victoria Nahmias[5], Michalis P. Kondylis[6], Dimitris Papahatjis[5], Zeta Daifoti-Papadopoulou[4] and Christina Spyraki[4]

[1]Laboratory of Behavioral Neuroscience, Department of Psychology, School of Social Sciences, University of Crete, 74100 Rethymnon; [2]Department of Pharmacology, Medical School, University of Ioannina, 45110 Ioannina; [3]Laboratory of Pharmacology, Department of Basic Sciences, Faculty of Medicine, University of Crete, 71110 Heraklion, Crete; [4]Department of Pharmacology, Medical School, University of Athens, 11527 Goudi, Athens; [5]Institute of Organic and Pharmaceutical Chemistry, National Hellenic Research Foundation, 11635, Athens; [6]Bristol-Myers Squibb, 146 71 Athens, Greece

Key words: Cannabinoid, agonist, CB1/CB2 receptors, binding, behavior

INTRODUCTION

Emerging evidence implicates endocannabinoids in a wide variety of physiological and pathophysiological processes. To date, most cannabinoid drugs used therapeutically are derived from cannabis and produce their effects by activation of cannabinoid receptors. However, the psychoactivity of these compounds has prevented their widespread acceptance in clinical practice. Newly developed cannabinoids may hold the promise of the development of useful and safe drugs. This study aimed to investigate the pharmacological characteristics of a novel derivative of THC, DPG-4.

METHODS

DPG-4 was evaluated for CB1/CB2 receptor affinity and activity using radioligand binding and functional studies. Specific behavioral and neurochemical indices were examined in order to assess cannabinoid activity. Behavioral paradigms such as open field test, bar test and intracranial self-stimulation were used with the aim to compare the profile of DPG-4 to that of WIN 55,212-2. Dopaminergic activity, in discrete rat brain regions such as the striatum nucleus accumbens and prefrontal cortex, was also examined following acute administration of DPG-4 and WIN 55,212-2.

RESULTS

DPG-4, displayed low nanomolar affinities for CB1/CB2 receptors and increased the basal [^{35}S]GTPgS binding with an EC_{50} value similar to that found for WIN 55,212-2. Preliminary data using the aforementioned behavioral paradigms show a specific behavioral profile reminiscent of a CB1 agonist. The neurochemical findings further support the agonist nature of DPG-4 for the CB1 receptor.

CONCLUSIONS

These data support that DPG-4 has high affinity and acts as an agonist for the CB1 receptor. Studies are in progress in order to elucidate the structure-activity relationship that might be useful in the development of substances with promising therapeutic value

[This study was supported by a GSRT-EU project YB60]