Drug Status Report

**Drug:** JWH-081

**Drug Name Status:** JWH-081 is the common name.

**Chemical Name:** 1-pentyl-3-(4-methoxy-1-naphthoyl)indole

**Other Names:** 4'-methoxy-1-pentyldiole; 4-methoxynaphthalen-1-yl-(1-pentylindol-3-yl)methanone

**Chemical structure:**

![Chemical structure of JWH-081](image)

**Molecular Formula:** C_{25}H_{25}NO_{2}

**Pharmacological class / Application:** Cannabinoid receptor agonist.

**International status:**

US: The substance is not listed on the schedules to the US Controlled Substances Act.

United Nations: The substance is not listed on the Yellow List - List of Narcotic Drugs under International Control nor the Green List - List of Psychotropic Substances under International Control.

Canadian Status: JWH-081 is one of several synthetic cannabimimetic substances that were synthesized to assess the binding affinities of a series of 3-(alkoxy-1-naphthoyl)indoles to the CB₁ and CB₂ receptors\(^1\). JWH-081 has a potent binding affinity for both the CB₁ and CB₂ receptors but its affinity for the CB₁ receptor is reported to be ten times greater than that for the

\(^1\)M M Aung et al. (2000) Influence of the –1 alkyl chain length of cannabimimetic indoles upon CB₁ and CB₂ receptor binding, Drug and Alcohol Dependence 60:133-140.
CB₂ receptor\textsuperscript{1,2}. Furthermore, a recent 3D-QSAR study of the selectivity of indole ligands for the CB₁ receptor identified JWH-081 as the most selective molecule for the CB₁ receptor of all the ligands that were investigated, and exceeded the selectivities observed for known potent cannabinoid agonists such as JWH-018 and JWH-015\textsuperscript{3}. These computational data support that JWH-081 has potential as an efficacious CB₁ receptor agonist.

The efficacy of many synthetic cannabinoids, particularly those that have a high binding affinity for the CB₁ receptor, is not readily available in the literature\textsuperscript{4}. This is mainly due to research efforts being focused upon developing drugs that do not produce unwanted psychoactive effects and hence more studies which evaluate the efficacy of substances that display a high binding affinity for the CB₂ receptor. However, unpublished \textit{in vivo} data in the mouse has shown JWH-081 to be a highly potent CB₁ receptor agonist\textsuperscript{5}.

Cannabinoid receptor agonists have been declared to be included within item 1 of Schedule II to the CDSA by virtue of being “similar synthetic preparations.” Cannabinoid receptor antagonists have been declared to fall outside item 1 of Schedule II to the CDSA. Given the high affinity and high selectivity of JWH-081 for the CB₁ receptors as well as \textit{in vivo} data showing the substance as a potent CB₁ agonist, JWH-081 should be included in item 1 of Schedule II.

Recommendation: JWH-081 is included in item 1 of Schedule II to the CDSA and is a controlled substance.

January 7\textsuperscript{th}, 2010


\textsuperscript{5} Personal communication (email correspondence attached).