Structure-Activity Relationship of Matrine Type Alkaloids Part 24; Synthesis and Antinociception of 3-Arylpiperidine Derivatives.

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We previously reported that (+)-matrine (**1**) and (+)-allomatrine (**2**), a typical matrine type lupine alkaloid isolated from some *Sophora* plants(Leguminosae), has the antinociceptive properties identical to those of pentazocine. The effects of **1** are mediated mainly through activation of □-opioid receptors and partially through □-opioid receptors, and these of **2** are mediated only through activation □-opioid receptors. Because the skeleton of matrine type alkaloid differ from those of conventional □-opioid receptor agonists, the structure-activity relationship of this antinociceptive effects are very interesting.

4-Dimethylamino-1-pentanoylpiperidine (**3**) was determined as a lead compound by identifying the partial structure of **1** for expressing the effects. Then we synthesized some derivatives of lead compound **3** and evaluated for these antinociceptive effects. This research gave important information that compound **4**, which had phenyl group on 3 position of piperidine ring, exert high antinociceptive effects compared to **3**. Taking this result, we attempted to synthesize the derivatives converted phenyl moiety of **4** and evaluate for these antinociception to find higher active compound. As a result, several derivatives of **4** having high antinociceptive effects were revealed.

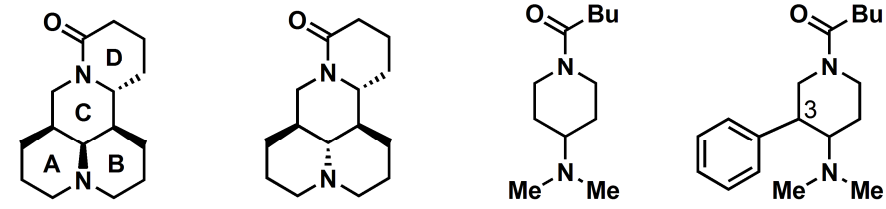

Figure. Structure of matrine derivatives.