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# Research Progress in Chemical Components and Pharmacological Effectiveness of *Piper hancei Maxim*

Lei Haipeng[1]*, Zhou Bin[2] and Chen Xianqiang[3]

[1]Department of Biology and Chemistry, City University of Hong Kong, Kowloon, Hong Kong, People's Republic of China

[2]School of Pharmacy, Jiangxi Science and Technology Normal University, Nanchang, PR China

[3]State Key Laboratory of Quality Research in Chinese Medicine and Institute of Chinese Medical Sciences, University of Macau, PR China

## RESEARCH ARTICLE

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***For Correspondence:**
Lei Haipeng, Department of Biology and Chemistry, City University of Hong Kong, Kowloon, Hong Kong, People's Republic of China, Tel: 34424490

E-mail: haipelei@cityu.edu.hk

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**ABSTRACT**

**Objective:** To compile the various research reporting active chemical components of *Piper hancei Maxim*, as well as their pharmacological effects.

**Results:** Up to now, the chemical components isolated from *Piper hancei* include mainly alkaloids, lignans etc. Pharmacological references show that it has antiplatelet activities, anti-inflammation, antimicrobial, antioxidation, antitumor and insecticidal activity.

**Conclusion:** To lay the basis of literature and inspired ideas on *Piper hancei*.

## INTRODUCTION

We live in an age where human health problems are changing dramatically. Modern medicine has greatly enhanced life expectancy and offered a cure for most of the deadliest communicable disease. Yet, because of the ageing population and increasingly unhealthy lifestyles, new crises are surfacing. Cardiovascular disorders, hypertension, cancers and diabetes appear today in unprecedented and alarming proportions. With the failure of classic medicinal methods to cure some of these new leading killer diseases, medicinal plants and natural products offer an alternative not to be overlooked.

Plants are already vital components of human diet, but are now becoming essential medicinal elements throughout the word as well. They represents the only medicinal alternative for many living in under-developed countries and although access to the modern medicine is not a problem in developed countries, an important proportion of the population also makes use of medicinal plants for historical and cultural reasons [1]. For these reasons, plants represent an important economic market whose growing popularity has naturally attracted the attention of scientist since decades [2].

With more than 1000 species represented in the *Piperaceae* family, a genus *Piper* is present in traditional medicine all over the world. Behind the notorious pepper spice lies a plant whose various biological effects have been reported to include antitumor, anticancer, anti-platelet aggregation, hepatotoxicity, hepatoprotective effects, anti-obesity, immune-enhancing and anti-inflammatory [3]. In the last few decades, several studies have been carried out in order to identify the biological actives compounds of these medicinal plants.

Of particular interest is *Piper hancei* Maxim., a piper species whose plants grow in forests, mostly by climbing on trees or rocks. It is distributed throughout Zhejiang, Fujian, Hubei, Guangdong, Guangxi, Yunnan province in china. The plant is currently

used to treat several illnesses including rheumatism, wind-cold, cough as well as more serious pathology such as influenza and dysmenorrhea [4].

The purpose of this review is to provide comprehensive information about the phytochemistry and the pharmacological effects of *Piper hancei* Maxim. A list of the 35 active compounds that have been found in *Piper hancei* are listed here, along with some of their most relevant biological activities, are listed here. These activities includes, not extensively, anti-platelet [5], anti-inflammatory [6,7], antibacterial [8], antioxidant [9,10], anticancer [11], cytotoxic effects [12,13].

Although these discoveries represent only the tip of the iceberg as to what has been gathered on *Piper hancei*, it compiles the most significant insights on the potential of the plant for medicinal applications. This review intends to provide an important resource for investigators planning future studies on this extraordinary plant.

## PHYTOCHEMICAL OF Piper hancei.

The chemical constituents of *Piper hancei* can be separated in three groups. The most prominent group of active species family regroups the alkaloids/amides molecules. A second group contains the lignans and neolignans compounds. The third group is a miscellaneous gathering of other actives molecules. These constituents of *Piper hancei* plant are summarized in **Tables 1, 2 and 3**, and their chemical structures are shown in **Figures 1, 2 and 3**.

Alongside the compounds listed in these tables, Lai *et al.* used GC-MS to analysis the essential oil from *Piper hancei* and identified 26 additional compounds from it, mostly terpenes and phenols. These compounds includes α-pinene, 1,8-cineole, linalool and terpinyl acetate whose percentage represent 56.45% of the oil composition [14]. These compounds are however not listed here.

### Alkaloids/Amides: Table 1 – Figure 1.

**Table 1**. Alkaloids/Amides.

| NO. | Name | CAS | Plant | Ref. |
|---|---|---|---|---|
| 1 | Futoamide | 23477-80-7 | Piper hancei<br>Piper longum<br>Piper wallichii | [15,16] |
| 2 | Piperlonguminin | 5950-12-9 | Piper hancei<br>Piper longum | [17,18] |
| 3 | Pellitorin | 18836-52-7 | Piper hancei<br>Piper cubeba | [19,20] |
| 4 | Cinnamamide | 20375-38-6 | Piper hancei | [21] |
| 5 | 2-Propenamide,3-(3-hydroxy-4-methoxyphenyl)-N-[2-(4-hydroxyphenyl)ethyl] | 640235-90-1 | Piper hancei | [12,15,22] |
| 6 | Trichostachine | 25924-78-1 | Piper hancei<br>Piper longum<br>Piper chaba<br>Piper arboreum | [23] |
| 7 | Nigrinodine | 259654-51-8 | Piper hancei | [24] |
| 8 | Retrofractamide A | 94079-67-1 | Piper hancei | [25] |
| 9 | Piperin | 94-62-2 | Piper hancei | [26,27] |
| 10 | Pipercide | 54794-74-0 | Piper hancei<br>Piper longum<br>Piper nigrum | [19,24,25] |
| 11 | Guineensine | 55038-30-7 | Piper hancei<br>Piper longum<br>Piper nigrum<br>Piper chaba | [25] |
| 12 | Trichostachine | 25924-78-1 | Piper hancei<br>Piper longum<br>Piper chaba | [23,28] |
| 13 | Piperovatine | 25090-18-0 | Piper hancei<br>Piper scutifolium<br>Piper piscatorum | [13] |
| 14 | Aristolactam A IIIa | 97399-91-2 | Piper hancei<br>Piper wallichii | [29-31] |
| 15 | Chingchengenamide A | 139906-29-9 | Piper hancei<br>Piper piscatorum<br>Piper laetispicum | [24,32] |
| 16 | Aristololactam A II a | 53948-07-5 | Piper hancei<br>Piper lolot<br>Piper kadsura | [6,30] |
| 17 | Piperolactam A | 112501-42-5 | Piper hancei | [33] |
| 18 | Piperolactam D | 128718-51-4 | Piper hancei | [33] |

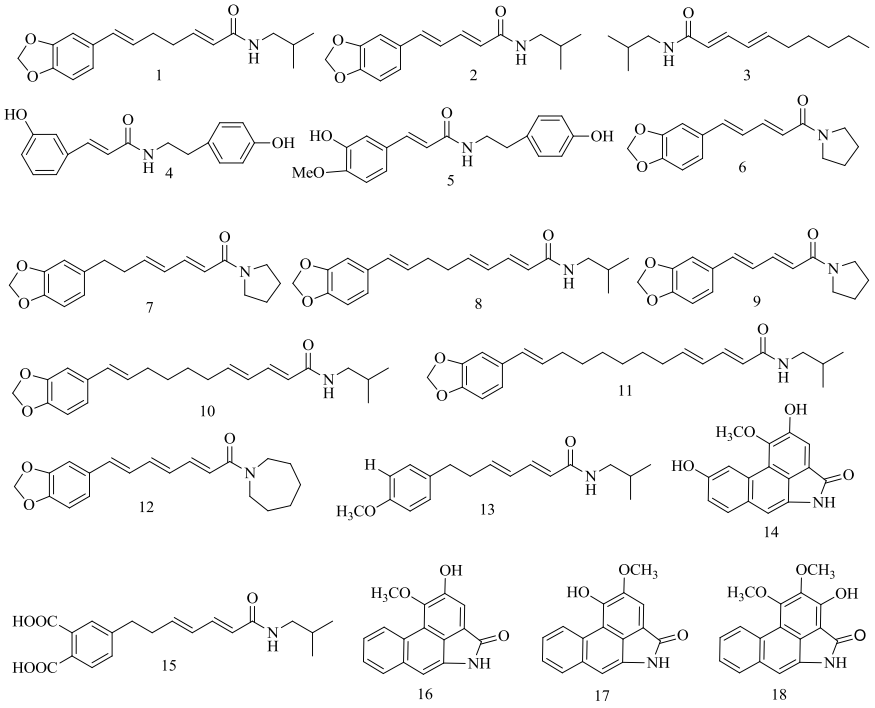

**Figure 1.** Chemical structure of compounds listed in Table 1.

## Lignans/Neolignans: Table 2 – Figure 2.

**Table 2.** Lignans/Neolignans.

| No. | name | CAS | Plants | Ref. |
|---|---|---|---|---|
| 19 | Hancinone B | 111843-09-5 | *Piper hancei*<br>*Piper wallichii* | [34] |
| 20 | Hancinone C | 111843-10-8 | *Piper hancei*<br>*Piper wallichii* | [5] |
| 21 | Kadsurenone | 95851-37-9 | *Piper hancei*<br>*Piper wallichii*<br>*Piper kadsura* | [29,35] |
| 22 | Denudatin B | 87402-88-8 | *Piper hancei*<br>*Piper wallichii*<br>*Piper clarkii* | [5,34] |
| 23 | Hancinone | 104013-61-8 | *Piper hancei*<br>*Piper wightii* | [36] |
| 24 | Hancinol | 108864-50-2 | *Piper hancei* | [37] |
| 25 | Burchellin | 38276-59-4 | *Piper hancei*<br>*Piper wallichii*<br>*Piper kadsura*<br>*Piper wightii* | [35,37] |
| 26 | Hancinone D | 104973-90-2 | *Piper hancei*<br>*Piper wallichii* | [5] |
| 27 | δ-Sesamin | 607-80-7 | *Piper hancei* | [33] |

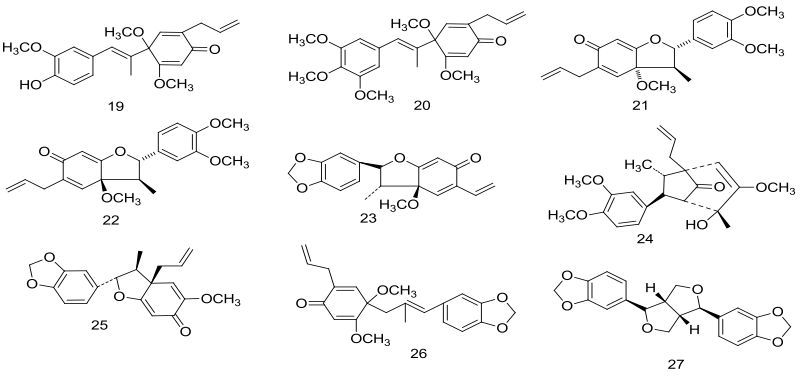

**Figure 2.** Chemical structure of compounds listed in Table 2.

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## Others: Table 3 – Figure 3.

**Tables 3.** Miscellaneous.

| No. | Name | CAS | Plants | Ref. |
|---|---|---|---|---|
| 28 | Crotepoxide | 20421-13-0 | *Piper hancei*<br>*Piper cubeba*<br>*Piper clarkia*<br>*Piper wightii*<br>*Piper kadsura* | [5] |
| 49 | β-Sitosterol | 83-46-5 | *Piper hancei* | [38] |
| 30 | Vanillic acid | 121-34-6 | *Piper hancei* | [9,39] |
| 31 | Veratric acid | 93-07-02 | *Piper hancei* | [8] |
| 32 | Daucosterin | 474-58-8 | *Piper hancei* | [40,41] |
| 34 | Syringic acid | 530-57-4 | *Piper hancei* | [42] |
| 33 | Stigmast-4-ene-3,6-dione | 23670-94-2 | *Piper hancei* | [43] |
| 35 | Hydroxychavicol | 1126-61-0 | *Piper hancei* | [33] |

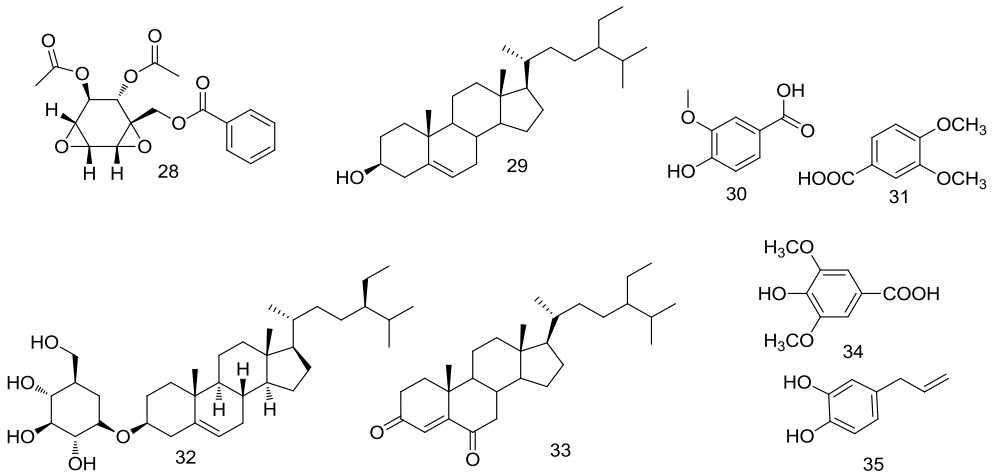


**Figure 3.** Chemical structure of compounds listed in Table 3.

# BIOLOGICAL ACTIVITY

## Antiplatelet Activity

Platelet-activating factors (PAF) are phospholipid molecules that are involved in the mediation of inflammation and patelet aggregation [34]. A couple of studies have reported the screening of large library of constituents from *Piper hancei* for their potential antiplatelet activity [5,35]. Han's group reported that Hancinone B, Hancinone C, Kadsurenone, Futoamide were PFA receptor antagonists. The ethanolic extract from *Piper hancei* was also reported to inhibit both PAF induced rabbit platelet aggregation and PAF induced inflammatory reaction [5,34].

## Anti-inflammatory Activity

Lin *et al.* reported that *Piper kadsura Ohwi*, which is always substituted for *Piper haicen* or *Piper puberulum* (Benth.) in the market, have anti-inflammatory activity [29,44]. Han *et al.* have found three compounds with anti-inflammatory activity from *Piper hancei*[10]. Kim evaluated the anti-neuroinflammatory activities by assessing nitric oxide (NO) production in LPS-activated BV-2 cells; a microglia cell line [6,7]. The result showed that Kadsurenone had anti-neuroinflammatory activities.

## Antimicrobial Activity

Pellitorin, Veratric acid, β-Sitosterol, Daucosterin and Stigmast-4-ene-3,6-dione which are found in *Piper hancei*, but *Piper cubeba*, *Piper retrofractum* and *Piper Sarmentoum*, all were found to have antimicrobial activities [8,45]. Pellitorin showed moderate to strong growth inhibition against Listeria monocytogenes, with (Minimum inhibitory concentration, MICs) between 62.5 and 125 μg/mL [46]. *In vitro* bioassay show that Daucosterin exhibited antibacterial activity [47]. Veratric acid showed the antibacterial activities mainly against gram positive germs [8].

## Antioxidant Activity

Crotepoxide, isolated from *Piper hancei* and the root of Panax notoginseng has been found to exhibit antioxidant activity [10]. Pajak *et al.* reported that vanillic acid showed antioxidant activity and evaluated using 2,2-azinobis (3-ethyl-benzothiazoline-6-sulfonic acid, (ABTS), 2,2-diphenyl-1-picrylhydrazyl (DPPH) and ferric reducing antioxidant power (FRAP) assays [9]. Furthermore, Yao's group studies shown that syringic acid also have antioxidant activity [42,48].

### Anticancer Activity

Do's group reported that piperine not only inhibited proliferation, but also HER2 gene expression at a transcriptional level. It also induces apoptosis through caspase-3 activation and PARP cleavage and was found to efficiently kill breast cancer cells [27]. Pradeep *et al.* studies showed that piperine have a dose-dependent anticancer activity against B16F-10 melanoma cell and inhibited transcription factors such as ATF-2, c-Fos and CREB [11].

### Cytotoxicity

Aristolactam A IIIa, Nigrinodine and Guineensine were found to have cytotoxic activity against human cervical carcinoma HeLa cells, as evaluated by three different cytotoxicity assays [12,13]. Nigrinodine showed cytotoxic activity against CCRF-CEM, HL-60, PC-3, P-388, HT-29, A549 and HA22T cells [49].

### Insecticidal Activity

Pipercide, isolated from *Piper hancei*, showed toxicity against female adults of Culex pipiens pallens and Aedesaegypti with an $LD_{50}$ value of 3.2 μg/female and 2.0 μg/female, respectively [50]. Piperovatine showed important antiprotozoal activity against the amastigote and promastigote forms of *L. amazonensis* [51].

### Other Biological Activity

Retrofractamide A and piperine were found to have a hepatoprotective effect on D-galactosamine (d-GalN)/lipopolysaccharide (LPS)-induced liver injury in mice. Guineensine was significantly inhibited anti-HBV against with Hep G 2.2.15 cell line *in vitro* [52]. Chingchengenamide A was shown to have antidepressant activity [32].

## CONCLUSIONS

Here, an attempt was made to compile relevant information about both the phytochemistry and the pharmacology of the *Piper hancei*. The review highlight's the medicinally significant constituents of the plant and provides a useful database for researchers in the field.

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