Since the beginning of human civilization, medicinal plants have been used by mankind for its therapeutic value. Nature has been a source of medicinal agents for thousands of years and an impressive number of modern drugs have been isolated from natural sources. Many of these isolations were based on the uses of the agents in traditional medicine. The plant-based, traditional medicine systems continue to play an essential role in health care, with about 80% of the world’s inhabitants relying mainly on traditional medicines for their primary health care.

In this study, I emphasized on the biologically active constituents of medicinal plants from Indonesia and Myanmar, especially on malaria and cancer diseases, which were major public health problems in Myanmar and are reported as the leading cause of morbidity and mortality.

*Caesalpinia crista* Linn. (Fabaceae) is a popular medicinal plant widely distributed throughout the tropical and subtropical regions of Southeast Asia. In Indonesia, it is commonly known as “Bagore” and the decoction of root has been praised for its important health benefits such as in the treatment of rheumatism, backache and as a tonic. Its seed kernels have been used by the people of local communities as an antimalarial and anthelmenthic drug. In Myanmar, this plant is locally known as “Ka-Lain” and its seeds are used as anthelmintic, antipyretic, anti-inflammatory, and antimalarial drug.

To discover anticancer agents from Myanmar medicinal plants based on anti-austerity strategy, 49 plants were collected from Pin-da-ya area, Shan state of Myanmar. The plants were selected on the basis of their ethnomedicinal use in Myanmar traditional medicine system. Among the tested extracts, four plant extracts, *Soymida febrifuga* Adr.Juss, *Vitex negundo* Linn., *Piper longum* Linn., and *Kayaea assiaca* King & Prain, exhibited...
100% preferential cytotoxicity against human pancreatic cancer PANC-1 cells under nutrient-deprived conditions at 10 µg/mL. Among the four active plants, *Soymida febrifuga* and *Vitex negundo* are selected for further phytochemical investigation.

1. Constituents of *Caesalpinia crista* Linn. and their anti-malarial activity1,2,3)

The CH2Cl2 extract of the seed kernels of *Caesalpinia crista* possessed a significant inhibitory activity of parasitemia level in mice infected with *Plasmodium berghei*. Thus, the CH2Cl2 extract was subjected to chemical examination which led to the isolation of thirty-six diterpenes. Among them, six were novel norcassane-type diterpenes, named as norcaesalpinins A (1), B (2), C (3), D (6), E (9) and F (13), and fourteen were new cassane-type diterpenes, caesalpinins C-D (4-5), E-F (7-8), G-I (10-12), J-P (14-20). To the best of our knowledge, 1, 2, 6, 9 and 13 are the first examples of 17-norcassane-type diterpenes, which may be biosynthesized through decarboxylation of C-17 of cassane-type diterpenes like caesalmin C (33). Similarly, 3 represents unprecedented 16-norcassane-type diterpene, probably derived from 2-acetoxy-3-deacetoxy- caesaldekarin e (21) isolated from the same extract, via oxidative cleavage of the C-15 double bond. Among the isolated compounds, 2-acetoxy-3-deacetoxycaesaldekarin e (21), 14(17)-dehydrocaesalpin F (25), 2-acetoxycaesaldekarin e (26), 7-acetxybonducellpin C (27), 3-deacetoxy-6-acetxycaesaldekarin e (30) and 14(17)-dehydro-a-caesalpin (31) were obtained from natural sources for the first time.

The isolated 16 cassane- and norcassane-type diterpenes, norcaesalpinins A-C (1-3), D (6), E (9), caesalpinins C-F (4-8), and known compounds 2-acetoxy-3-deacetoxycaesaldekarin e (21), caesalmin B (22), caesaldekarin e (23), 14(17)-dehydrocaesalpin F (25), 2-acetoxycaesaldekarin e (26), 7-acetxybonducellpin C (27), caesalmin G (28), have been tested for their growth inhibitory against the malaria parasite, *Plasmodium falciparum* FCR-3/2A clone, in
Among them, norcaesalpinin E (9) exhibited the most potent activity with an IC\textsubscript{50} value of 0.09 µM, which was stronger than that of chloroquine (IC\textsubscript{50}, 0.28-0.29 µM), a well-known antimalarial drug. Norcaesalpinin A (1), a major compound isolated from C. crista in this study, displayed the inhibitory activities with IC\textsubscript{50} value of 0.80 µM. Due to its amount available 1 was further tested for in vivo activity, using antimalarial exoerthrocytic schizontocidal assay. At a doses of 10, 1 and 0.1 mg/kg (p.o.), 1 significantly suppressed the parasitemia by 48.0, 40.9 and 33.0%, respectively. At the same concentrations, artemisinin, a known antimalarial drug was used as a positive control, reduced parasitemia by 65.5, 37.4 and 26.9%, respectively. These results suggested that the antimalarial activity of the CH\textsubscript{2}Cl\textsubscript{2} extract of C. crista may be due to diterpene constituents which could support the traditional medicine use as an antimalarial drug.

2. Constituents of *Soymida febrifuga* and their cytotoxic activity\textsuperscript{4)}

*Soymida febrifuga* A. Juss, English name “Indian red wood”, belongs to the family Meliaceae. It is locally known as Dan-Tagu-ni and is distributed in the Bago Division, Mandalay Division and Shan State of Myanmar. In Ayurveda medicine its wood is used to remove ‘vata’, cures for tridosha, fever, cough, asthma, blood impurities, ulcers, leprosy and dysentery. In Unani system it is astringent to bowels and useful in fever. It is bitter tonic, antiperiodic and antimalerials. It is used in the form of decoction for rheumatic swellings.

The 70% ethanol extract of *Soymida febrifuga* was found to kill PANC-1 human pancreatic cancer cells preferentially under nutrition-deprived conditions at a concentration of 10 µg/mL. Phytochemical investigation led to the isolation of 27 compounds including four new compounds [(3\textsuperscript{R})-6,4′-dihydroxy-8-methoxy-homoisoflavan (37), (2\textsuperscript{R})-7,4′-dihydroxy-5-methoxy-8-methylflavan (38), 7-hydroxy-6-methoxy-3-(4′-hydroxybenzyl)coumarin (39), and 6-hydroxy-7-methoxy-3-(4′-hydroxybenzyl) coumarin (40)]. 2′,4′-Dihydroxychalcone (44) displayed the most potent preferential cytotoxicity (PC\textsubscript{50} 19.0 µM) against PANC-1 cells. The isolated compounds were tested against the panel of five additional cancer cell lines [colon carcinoma (colon 26-L5), melanoma (B16-BL6), lung adenocarcinoma (A549), cervix HeLa adenocarcinoma (HeLa), and fibrosarcoma (HT-1080)], and their structure-activity relationships were determined. The cytotoxic activity of 4′-hydroxy-3,5-dimethoxystilbene (42) against colon 26-L5 (IC\textsubscript{50} 2.96 µM) was found to be stronger than the positive control, doxorubicin, (IC\textsubscript{50} 3.12 µM).

3. Constituents of *Vitex negundo* Linn. and their cytotoxic activity\textsuperscript{5)}

*Vitex negundo* Linn. is belonging to the family Verbenaceae and is a well-known aromatic shrub or ever green small tree. It is commonly known as Kyaung-pan-gyi in Myanmar and English name is “Five leaved chaste tree”. The plant has
long spires of pale lilac or rose-colored flowers and small gray-brown, hard fruits, which has a pepper-like aroma and flavor which is the part used medicinally. The plant extract have been widely used for the treatment of a large number of human ailments. The chemical entities of this plant have been used as an antidiabetic, antibacterial, anti-inflammatory, antifungal, antinociceptive, anti androgenic, anticonvulsant, antioxidant, and anti-tumor agents. The ethanol extract of V. negundo showed preferential cytotoxicity against PANC-1 cells in NDM in a concentration-dependent manner, with 100% cell death at the concentration of 10 µg/mL in NDM. Isolated compounds, chrysoplenetin (64) and chrysosplenol D (65), were tested for their preferential cytotoxicity in vitro. They exhibited potent preferential cytotoxicity in a concentration-dependent manner with PC50 value of 3.4 µg/mL (for 64) and 4.6 µg/mL (for 65) and showed 100% cytotoxicity at the concentration of 10 µg/mL. The most active compound, chrysoplenetin (64), was further evaluated against a panel of 39 human cancer cell lines (JFCR-39). In JFCR-39 panel, lung NCI-H522, ovarian OVCAR-3 and prostate PC-3 cells were found to be most sensitive with GI50 0.12, 0.18 and 0.17 µM, respectively. The COMPARE analysis suggested that the molecular mode of action of chrysoplenetin (64) was unique as compared with the existing anticancer drugs. Vitex negundo Linn. and its active constituents might have possible beneficial effects for the patients suffering from cancer in a real clinical situation.

In conclusion, norcaesalpinin E (9) has significant antimalarial activity (in vitro) which were less than a well-known antimalarial drug, chloroquine. In addition, one of the major constituent of the Caesalpinia crista, norcaesalpinin A (1), has significant antimalarial activity (in vivo) as a well-known antimalarial drug artemisinin. These compounds from the Caesalpinia crista could support the development of antimalarial agents in malaria treatment in future. 2′,4′-Dihydroxychalcone (44) from Soymida febrifuga displayed the most potent preferential cytotoxicity (PC50 19.0 µM) against PANC-1 cells. On the other hand, the cytotoxic activity of 4′-hydroxy-3,5-dimethoxystilbene (42) against colon 26-L5 (IC50 2.96 µM) was found to be stronger than the positive control, doxorubicin (IC50 3.12 µM). The preferential cytotoxicity exhibited by these compounds could support future clinical trial on cancer therapy. Vitex negundo Linn. and its active constituents also might have possible beneficial effects for the patients suffering from cancer in a real clinical situation.

[References]


Chart 1. Structure of compounds (1-36) isolated from the CH₂Cl₂ extract of seed kernels of *Caesalpinia crista* Linn.

Chart 2. Structure of compounds (37-63) isolated from the bark of *Soymideebrfaga*.

Chart 3. Structure of compounds (64-65) isolated from the fruit of *Vitex negundo*.