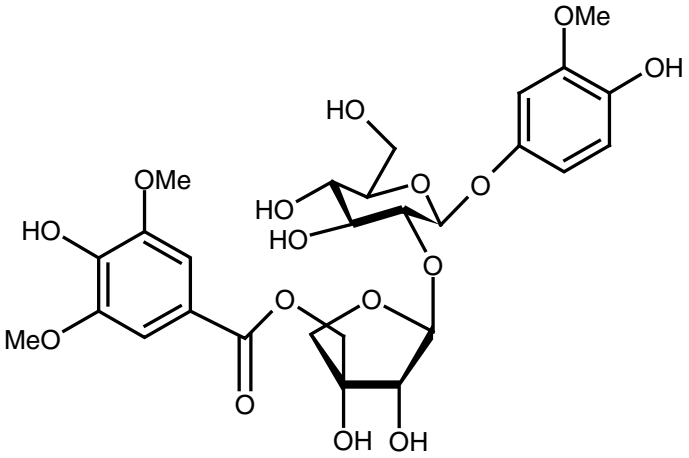
Physical data: $C_{27}H_{34}O_{16}$, amorphous powder, $[\alpha]_D^{20}$ +3.29° (MeOH, *c* 0.002)

Structure:



Albibrissinoside B

Compound class: Phenolic glycoside

Source: *Albizia julibrissin* Durazz. (stem barks; family: Leguminosae)

Pharmaceutical potential: ***Antioxidant***
The phenolic glycoside exhibited *in vitro* antioxidant activity – it displayed free radical scavenging activity (evaluated in 1,1-diphenyl-2-picrylhydrazyl assay) with IC_{50} value of 10.2 μM; the activity was found to be more potent that of L-ascorbic acid used as positive control ($IC_{50} = 10.4$ μM).

Reference

Jung, M.J., Kang, S.S., Jung, Y.J., and Choi, J.S. (2004) *Chem. Pharm. Bull.*, **52**, 1501.

Albizosides A–C

Systematic names:

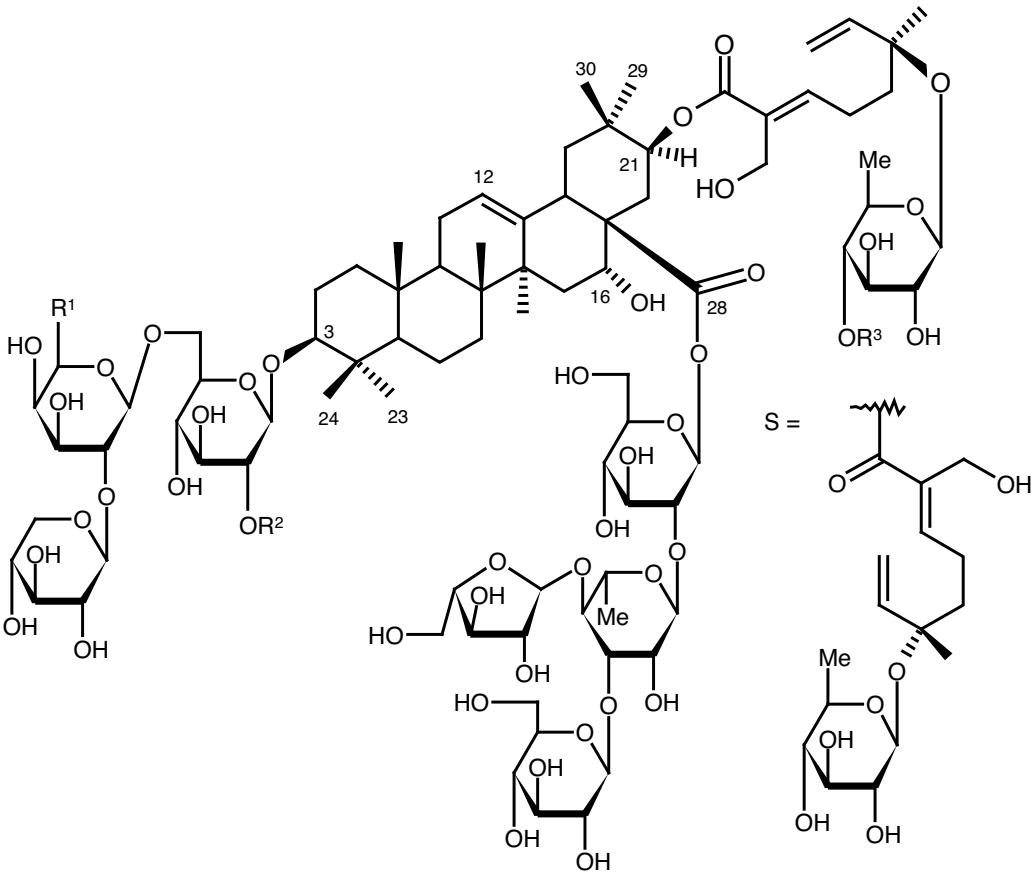
- Albizoside A: 21-*O*-{(2*E*,6*S*)-2-hydroxymethyl-6-methyl-6-*O*-{4-*O*-(2′*E*,6′*S*)-2′,6′-dimethyl-6′-*O*-[2′-*O*-(2″*E*,6″*S*)-2″-hydroxymethyl-6″-methyl-6″-*O*-β-D-quinovopyranosyl-2″,7″-octadienoyl-β-D-quinovopyranosyl]-2′,7′-octadienoyl-β-D-quinovopyranosyl}-2,7-octadienoyl}-3-*O*-[β-D-xylopyranosyl-(1→2)-β-D-fucopyranosyl-(1→6)-β-D-glucopyranosyl] acacic acid 28-*O*-β-D-glucopyranosyl-(1→3)-[α-L-arabinofuranosyl-(1→4)]-α-L-rhamnopyranosyl-(1→2)-β-D-glucopyranosyl ester
- Albizoside B: 21-*O*-{(2*E*,6*S*)-2-hydroxymethyl-6-methyl-6-*O*-{4-*O*-(2′*E*,6′*S*)-2′,6′-dimethyl-6′-*O*-[2′-*O*-(2″*E*,6″*S*)-2″-hydroxymethyl-6″-methyl-6″-*O*-β-D-quinovopyranosyl-2″,7″-octadienoyl-β-D-quinovopyranosyl]-2′,7′-octadienoyl-β-D-quinovopyranosyl}-2,7-octadienoyl}-3-*O*-{β-D-xylopyranosyl-(1→2)-β-D-fucopyranosyl-(1→6)-[β-D-glucopyranosyl-(1→2)]-β-D-glucopyranosyl} acacic acid 28-*O*-β-D-glucopyranosyl-(1→3)-[α-L-arabinofuranosyl-(1→4)]-α-L-rhamnopyranosyl-(1→2)-β-D-glucopyranosyl ester

- Albizoside C: 21-*O*-{(2*E*,6*S*)-2-hydroxymethyl-6-methyl-6-*O*-[4-*O*-(2′*E*,6′*S*)-2′,6′-dimethyl-6′-*O*-β-D-quinovopyranosyl-2′,7′-octadienoyl-β-D-quinovopyranosyl]-2,7-octadienoyl}-3-*O*-{β-D-xylopyranosyl-(1→2)-β-D-arabinopyranosyl-(1→6)-[β-D-glucopyranosyl-(1→2)]-β-D-glucopyranosyl} acacic acid 28-*O*-β-D-glucopyranosyl-(1→3)-[α-L-arabinofuranosyl-(1→4)]-α-L-rhamnopyranosyl-(1→2)-β-D-glucopyranosyl ester

Physical data:

- Albizoside A: $C_{118}H_{186}O_{56}$, white amorphous powder, $[\alpha]_D^{20}$ −34.4° (MeOH, *c* 0.09)
- Albizoside B: $C_{124}H_{196}O_{61}$, white amorphous powder, $[\alpha]_D^{20}$ −22.0° (MeOH, *c* 0.15)
- Albizoside C: $C_{107}H_{170}O_{54}$, white amorphous powder, $[\alpha]_D^{20}$ −16.0° (MeOH, *c* 0.25)

Structures:



Albizoside A: R^1 = M, R^2 = H, R^3 = S

Albizoside B: R^1 = Me, R^2 = GLc, R^3 = S

Albizoside C: R^1 = H, R^2 = GLc, R^3 = H

Glc: β-D-glucopyranosyl

Compound class: Triterpenoid saponins

Source: *Albizia chinensis* (Osb.) Merr. (stem barks; family: Leguminosae)

Pharmaceutical potential: ***Cytotoxic (antitumor)***
Albizosides A–C were evaluated for their cytotoxic activities against a small panel of human tumor cell lines such as HCT-8, Bel-7402, BGC-823, A549, and A2780 and were found to possess potent antitumor activity. The respective IC_{50} values against the cell lines (namely, HCT-8, Bel-7402, BGC-823, A549, and A2780) were determined to be 5.6, 2.6, 1.6, 1.9, and 1.3 μM for albizoside A; 1.3, 1.3, 3.8, 0.3, and 1.2 μM for albizoside B; 0.4, 0.4, 1.7, 0.01, and 0.3 μM for albizoside C; 3.2, 12.5, 9.7, 3.1, and 0.3 μM for camptothecin (positive control). However, the saponins showed hemolytic activity as evaluated on rabbit erythrocytes in the concentration range 0.01–100 μM; albizosides A–C exhibited the hemolytic activity with HC_{50} values of 0.4, 0.7, and 0.7 μM, respectively. The investigators suggested from structure–activity relationships that the second monoterpene-quinovopyranosyl moiety is involved in mediating the hemolytic activity of the saponins.

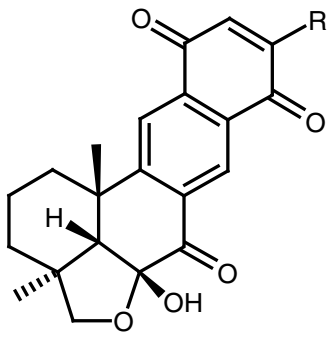
Reference

Liu, R., Ma, S., Yu, S., Pei, Y., Zhang, S., Chen, X., and Zhang, J. (2009) *J. Nat. Prod.*, **72**, 632.

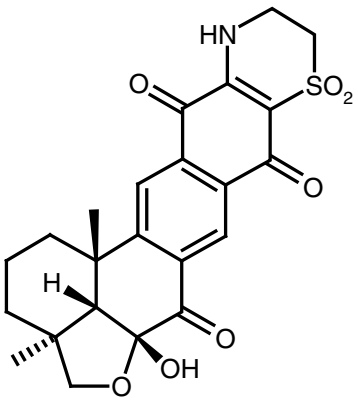
Alisiaquinones A–C and alisiaquinol

Physical data:
- Alisiaquinone A: $C_{21}H_{20}O_5$, yellow-brown powder, $[\alpha]_D^{25}$ −40° ($CHCl_3$, *c* 0.2)
- Alisiaquinone B: $C_{22}H_{22}O_6$, yellow-brown powder, $[\alpha]_D^{25}$ −27° ($CHCl_3$, *c* 0.3)
- Alisiaquinone C: $C_{23}H_{23}NO_7S$, yellow powder, $[\alpha]_D^{25}$ −75° ($CHCl_3$, *c* 0.2)
- Alisiaquinol: $C_{21}H_{22}O_5$, brown powder, $[\alpha]_D^{25}$ +90° ($CHCl_3$, *c* 0.2)

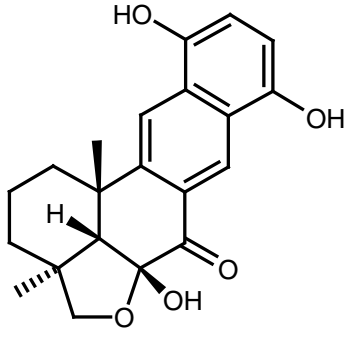
Structures:



Alisiaquinone A: R = H
Alisiaquinone B: R = OCH_3



Alisiaquinone C



Alisiaquinol

Compound class: Meroterpenoids

Source: A new Caledonian deep water sponge (a voucher specimen accessing number ORSTOM-R1514 is deposited at the Museum National d'Histoire Naturelle de Paris, France) as reported

Pharmaceutical potential: ***Antimalarial***

The present investigators evaluated alisiaquinones A–C and alisiaquinol as antimalarial chemotypes – the isolates exhibited micromolar range activity on two enzymatic targets of importance for controlling malaria, the plasmodial kinase Pfnek-1, and a protein farnesyl transferase (PFTase), as well as on different chloroquine-sensitive and -resistant strains of *Plasmodium falciparum*; alisiaquinone C was found to show a submicromolar activity on *P. falciparum*. Pfnek-1 activity was completely inhibited with alisiaquinone A and alisiaquinol at 50 μM, whereas alisiaquinone C was a poor inhibitor of the kinase.

Alisiaquinones A and B and alisiaquinol displayed similar activities *in vitro* on *P. falciparum*; however, alisiaquinone A was found to be slightly less cytotoxic. Alisiaquinone C, bearing the taurine substituent, showed a much better *in vitro* activity on *P. falciparum*, correlated with a better activity on PFTase, no activity on Pfnek-1, but a much higher selectivity index than the other compounds, especially on the chloroquine-resistant strain PfFcMC29. These results, especially the loss of activity of the hindered quinone system, suggest that the quinone/phenolic part of these compounds plays an important role in their mode of action on the ser/thr kinase Pfnek-1, but not on the PFTase, as all of the four compounds display micromolar range activity. However, the modification of the furan ring does not affect the activity very much, as shown by the comparison with xestoquinone.

The investigators also studied on the *in vivo* activity of all the isolates on rodent malaria; the compounds were found to reduce the parasitemia by 50% at 5 mg/kg; however, they displayed a relatively high level of toxicity with 100 and 80% mortality at 20 mg/kg, thus precluding further antimalarial development.

Reference

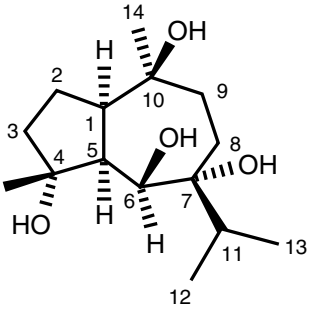
Desoubzdanne, D., Marcourt, L., Raux, R., Chevalley, S., Dorin, D., Doerig, C., Valentin, A., Ausseil, F., and Debitus, C. (2008) *J. Nat. Prod.*, **71**, 1189.

Alismorientol A

Systemic name: 4α,6β,7α,10β-Tetrahydroxy-1,5-*cis*-guaiane

Physical data: $C_{15}H_{28}O_4$, colorless prisms, mp 186.5–189 °C, $[\alpha]_D^{18.6}$ +22.17° (MeOH, *c* 0.2)

Structure:



Alismorientol A

Compound class: Sesquiterpenoid

Source: *Alisma orientalis* (Sam.) Juzep (rhizomes; family: Alismataceae)

Pharmaceutical potential: ***Antihepatitis B virus (anti-HBV)***
Alismorientol A was evaluated for its antihepatitis B virus (HBV) activity *in vitro* using Hep G 2.2.15 cell line; the investigators observed that the compound possesses moderate anti-HBV activity through suppressing HBV surface antigen (HBsAg) and HBVe antigen (HBeAg) secretions, with respective IC_{50} values of 1.1 and 14.7 μM.

Reference

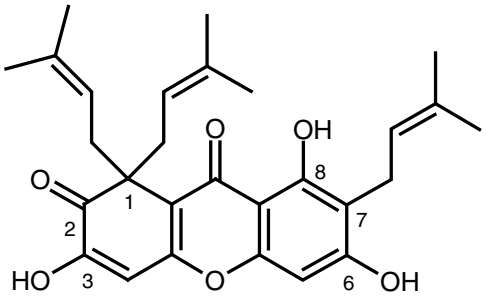
Jiang, Z.-Y., Zhang, X.-M., Zhou, J., Zhang, F.-X., Chen, J.-J., Lu, Y., Wu, L., and Zheng, Q.-T. (2007) *Chem. Pharm. Bull.*, **55**, 905.

Allanxanthone C

Systematic name: 1,2-Dihydro-3,6,8-trihydroxy-1,1,7-tri(3-methylbut-2-enyl)xanthen-2,9-dione (3-hydroxyapetalinone C)

Physical data: $C_{28}H_{32}O_6$, sticky yellow oil

Structure:



Allanxanthone C

Compound class: Prenyalted xanthone

Source: *Allanblackia monticola* Staner L.C. (stem barks; family: Clusiaceae)

Pharmaceutical potentials: ***Antiplasmodial; cytotoxic***
The isolate was evaluated for its antiplasmodial activity against two strains of *Plasmodium falciparum*, F32 (chloroquine sensitive) and FcM29-Cameroon (chloroquine resistant); the test compound was found to exhibit significant *in vitro* antiplasmodial potential against both the strains with respective IC_{50} values of 3.2 ± 0.0 and 2.6 ± 0.9 μg/ml at the 24 h, and 3.2 ± 0.3 and 0.6 ± 0.02 μg/ml at the 72 h after administration. Besides, the xanthone showed weak *in vitro* cytotoxicity against human melanoma cells (A375) with IC_{50} value of 83.8 ± 7.1 μg/ml estimated at the 24 h after application.

Reference

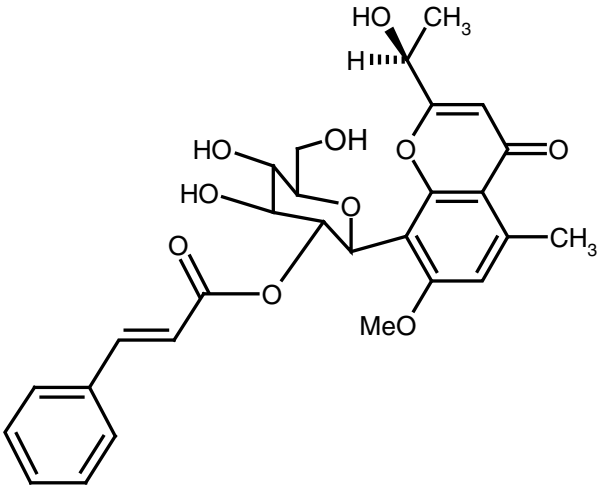
Azebaze, A.G.B., Meyer, M., Valentin, A., Nguemfo, E.L., Fomum, Z.T., and Nkengfack, A.E. (2006) *Chem. Pharm. Bull.*, **54**, 111.

Aloe C-glucosylchromone

Systematic name: 8-[*C*-β-D-[2-O-(*E*)-cinnamoyl]glucopyranosyl]-2-[(*R*)-2-hydroxypropyl]-7-methoxy-5-methylchromone

Physical data: $C_{28}H_{30}O_{10}$, off-white solid, mp 138–139 °C

Structure:



Aloe *C*-glucosylchromone

Compound class: *C*-Glucosylchromone

Source: *Aloe barbadensis* Mill. (leaves; family: Liliaceae)

Pharmaceutical potential: ***Anti-inflammatory***
The *C*-glucosylchromone was evaluated for topical anti-inflammatory activity using *in vivo* mouse assay; the test compound was found to have ability to reduce croton oil-induced ear inflammation comparable to that of hydrocortisone. At a dose of 200 μg/mouse ear, the compound afforded topical anti-inflammatory activity equivalent to 200 μg/ear of hydrocortisone at 6 h after treatment. Interestingly, there was found no reduction in thymus weight caused by treatment with the chromone glycoside for any of the doses tested while 200 μg/ear of hydrocortisone resulted in a 50% decrease in thymus weight.

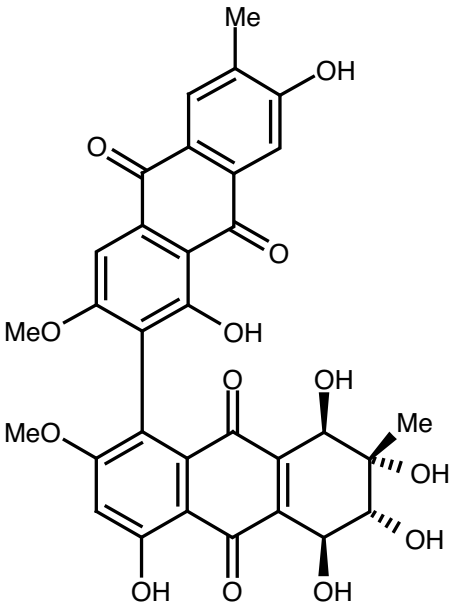
Reference

Hutter, J.A., Salman, M., Stavinoha, W.B., Satsangi, N., Williams, R.F., Streeper, R.T., and Weintrau, S.T. (1996) *J. Nat. Prod.*, **59**, 541.

Alterporriols G and H

Physical data: Alterporriols G and H: obtained as an inseparable 4: 3 mixture, $C_{32}H_{26}O_{13}$, red powder, $[\alpha]_D^{22}$ −316° (EtOH, *c* 0.05)

Structures:



Alterporriols G and H (atropisomers)

Compound class: Alterporriol-type anthraquinoid dimers

Source: *Stemphylium globuliferum* (an endophytic fungus isolated from stem tissues of the Moroccan medicinal plant *Mentha pulegium* L. (plant family: Lamiaceae))

Pharmaceutical potentials: ***Cytotoxic (antitumor); inhibitor of kinase enzyme activity***
The mixture of alterporriols G and H exhibited significant *in vitro* cytotoxicity against L5178Y cells with an EC_{50} value of 2.7 μg/ml; in addition, the mixture of the secondary metabolites was also evaluated to possess potent kinase inhibitory activity in an assay involving 24 different kinases, displaying EC_{50} values between 0.64 and 1.4 μg/ml toward individual kinases.

Reference

Debbab, A., Aly, A.H., Edrada-Ebel, R., Wray, V., Muller, W.E.G., Totzke, F., Zirrgiebel, U., Schachtele, C., Kubbutat, M.H.G., Lin, W.H., Mosaddak, M., Hakiki, A., Proksch, P., and Ebel, R. (2009) *J. Nat. Prod.*, **72**, 626.

Alvaradoins E–N

Systematic names:

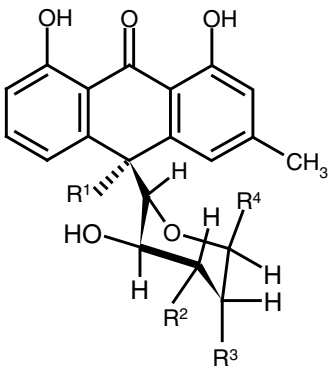
- Alvaradoin E: (10*S*)-*C*-(1-*O*-acetyl)-β-L-lyxopyranosyl-1,8-dihydroxy-3-methylanthracen-9(10*H*)-one
- Alvaradoin F: (10*R*)-*C*-(1-*O*-acetyl)-β-L-lyxopyranosyl-1,8-dihydroxy-3-methylanthracen-9(10*H*)-one
- Alvaradoin G: (10*R*)-*C*-(1-*O*-acetyl-3-*O*-senecioyl)-β-L-lyxopyranosyl-1,8-dihydroxy-3-methylanthracen-9(10*H*)-one

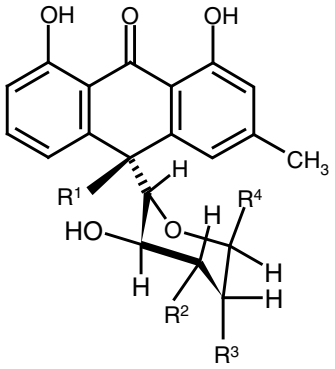
- Alvaradoin H: (10*S*)-*C*-(1-*O*-acetyl-3-*O*-senecioyl)-β-L-lyxopyranosyl-1,8-dihydroxy-3-methylanthracen-9(10*H*)-one
- Alvaradoin I: (10*R*)-*C*-(1-*O*-acetyl-3-*O*-senecioyl)-β-L-lyxopyranosyl-1,8,10-trihydroxy-3-methylanthracen-9-one
- Alvaradoin J: (10*S*)-*C*-(1-*O*-acetyl-3-*O*-senecioyl)-β-L-lyxopyranosyl-1,8,10-trihydroxy-3-methylanthracen-9-one
- Alvaradoin K: (10*R*)-*C*-(2-*O*-senecioyl)-β-L-lyxopyranosyl-1,8-dihydroxy-3-methylanthracen-9(10*H*)-one
- Alvaradoin L: (10*S*)-*C*-(2-*O*-senecioyl)-β-L-lyxopyranosyl-1,8-dihydroxy-3-methylanthracen-9(10*H*)-one
- Alvaradoin M: (10*S*)-*C*-(3-*O*-senecioyl)-β-L-lyxopyranosyl-1,8-dihydroxy-3-methylanthracen-9(10*H*)-one
- Alvaradoin N: (10*S*)-*C*-(1-*O*-acetyl)-β-L-lyxopyranosyl-1,8,10-trihydroxy-3-methylanthracen-9-one

Physical data:

- Alvaradoin E: $C_{22}H_{22}O_9$, yellow solid, mp 194–196 °C, $[\alpha]_D$ −16.8° (MeOH, *c* 0.07)
- Alvaradoin F: $C_{22}H_{22}O_9$, yellow solid, mp 210–213 °C, $[\alpha]_D$ −107.7° (MeOH, *c* 0.05)
- Alvaradoin G: $C_{27}H_{28}O_{10}$, brown solid, mp 197–200 °C, $[\alpha]_D$ −85.0° (MeOH, *c* 0.06)
- Alvaradoin H: $C_{27}H_{28}O_{10}$, yellow solid, mp 240–243 °C, $[\alpha]_D$ −26.0° (MeOH, *c* 0.05)
- Alvaradoin I: $C_{27}H_{28}O_{11}$, yellow solid, mp 148–149 °C, $[\alpha]_D$ −11.7° (MeOH, *c* 0.06)
- Alvaradoin J: $C_{27}H_{28}O_{11}$, yellow solid, mp 138–139 °C, $[\alpha]_D$ −56.7° (MeOH, *c* 0.05)
- Alvaradoin K: $C_{25}H_{26}O_9$, yellow solid, mp 143–144 °C, $[\alpha]_D$ −65.0° (MeOH, *c* 0.06)
- Alvaradoin L: $C_{25}H_{26}O_9$, yellow solid, mp 141–142 °C, $[\alpha]_D$ −26.7° (MeOH, *c* 0.09)
- Alvaradoin M: $C_{25}H_{26}O_9$, yellow solid, mp 153–154 °C, $[\alpha]_D$ −32.0° (MeOH, *c* 0.05)
- Alvaradoin N: $C_{22}H_{22}O_{10}$, yellow solid, mp 139–140 °C, $[\alpha]_D$ −56.0° (MeOH, *c* 0.05)

Structures:





Alvaradoin E: R^1 = H, R^2 = R^3 = OH, R^4 = —OOCCH$_3$

Alvaradoin F: R^1 = H, R^2 = R^3 = OH, R^4 = —OOCCH$_3$

Alvaradoin H: R^1 = H, R^2 = —OOCCH=C(CH$_3$)$_2$, R^3 = OH, R^4 = —OOCCH$_3$

Alvaradoin G: R^1 = H, R^2 = —OOCCH=C(CH$_3$)$_2$, R^3 = OH, R^4 = —OOCCH$_3$

Alvaradoin I: R^1 = R^3 = OH, R^2 = —OOCCH=C(CH$_3$)$_2$, R^4 = —OOCCH$_3$

Alvaradoin J: R^1 = R^3 = OH, R^2 = —OOCCH=C(CH$_3$)$_2$, R^4 = —OOCCH$_3$

Alvaradoin L: R^1 = H, R^2 = R^4 = OH, R^3 = —OOCCH=C(CH$_3$)$_2$

Alvaradoin K: R^1 = H, R^2 = R^4 = OH, R^3 = —OOCCH=C(CH$_3$)$_2$

Alvaradoin M: R^1 = H, R^3 = R^4 = OH, R^2 = —OOCCH=C(CH$_3$)$_2$

Alvaradoin N: R^1 = R^2 = R^3 = OH, R^4 = —OOCCH$_3$

Compound class: Anthracenone *C*-glycosides

Source: *Alvaradoa haitiensis* Urb. (leaves; family: Picramniaceae) [1]

Pharmaceutical potentials: ***Antitumor; cytotoxic; antileukemic***

The investigators evaluated *in vitro* cytotoxic activity of all the isolated compounds, alvaradoins E–N, in the KB cell line (human oral epidermoid carcinoma) using camptothecin as the reference standard. All of them displayed significant cytotoxicity with respective EC_{50} values of 0.050 ± 0.019, 0.065 ± 0.026, 0.65 ± 0.15, 1.07 ± 0.43, 12.5 ± 3.03, 15.9 ± 3.41, 0.27 ± 0.072, 0.59 ± 0.10, 0.38 ± 0.043, and $2.94 \pm 1.30\,\mu M$, while the EC_{50} value of the standard was found to be $0.0036 \pm 0.0029\,\mu M$. Among the test compounds, alvaradoins E and F were the most cytotoxic, having EC_{50} values that were only an order of magnitude less than that of the positive control, camptothecin. The most potent compounds in the *in vitro* assays (alvaradoins E and F) were further evaluated using the *in vivo* P388 (murine lymphocytic leukemia model) model, and modest *in vivo* activity against intraperitoneal (i.p.) implanted P388 xenografts (i.e., antileukemic activity of 125% T/C) was observed with alvaradoin E when mice were injected via the intraperitoneal route daily for 5 days per week at an optimal dose of 0.2 mg/kg body weight per injection; under the same conditions, alvaradoin F was found to be less active (115% T/C). This indicates that alvaradoin E bears the preferred stereochemistry, and that is why it is under consideration for further evaluation, possibly via derivatization and/or analogue development of the lead pharmacophore. The investigators also pointed out that in a more rigorous model of chemotherapy, where both the cancer cells and the treatment were imposed intravenously in a similar P388 assay, both compounds were found to be inactive, thereby suggesting metabolic degradation or other issues that influence drug distribution or accessibility of leukemia cells in bone marrow [2].

On the basis of the degree of cytotoxicity exhibited by the anthracenone *C*-glycosides, the research group [1] suggested a preliminary structure–activity relationship (SAR). In alvaradoins G and H, where the hydroxy at R^2 of the glycoside of alvaradoins E and F has been esterified as a 3-methylbut-2-enoyl moiety, the EC_{50} values increased by another order of magnitude. Similar results were observed in compounds alvaradoins K, L, and M, where an identical conversion was done at R^3 (alvaradoins K and L) or R^2 (alvaradoin M) of the glycoside and the R^4 acetate was converted to a hydroxy moiety. Cytotoxic efficacy of the compounds alvaradoins I, J, and N, where a hydroxy was inserted at C-10 of the anthracenone, was found to be reduced effectively. Further, the complete inactivity of chrysophanol (1,8-dihydroxy-3-methylanthracen-9(10*H*)-one, a previously known compound also isolated from this plant source by this research group), which structurally represents the core anthracenone aglycone of alvaradoin E–N, conclusively suggests that a combination of the anthracenone and glycoside units is essential for their cytotoxic activity.

References

[1] Phifer, S.S., Lee, D., Seo, E.-K., Kim, N.-C., Graf, T.N., Kroll, D.J., Navarro, H.A., Izydore, R.A., Jiménez, F., Garcia, R., Rose, W.C., Fairchild, C.R., Wild, R., Soejarto, D.D., Farnsworth, N.R., Kinghorn, A.D., Oberlies, N.H., Wall, M.E., and Wani, M.C. (2007) *J. Nat. Prod.*, **70**, 954.

[2] Mi, Q., Lantvit, D., Reyes-Lim, E., Chai, H., Phifer, S.S., Wani, M.C., Wall, M.E., Tan, G.T., Cordell, G.A., Farnsworth, N.R., Kinghorn, A.D., and Pezzuto, J.M. (2005) *Anticancer Res.*, **25**, 779.