Natural Products Published in 2009 from Plants Traditionally Used to Treat Malaria

Authors Joanne Bero, Joëlle Quetin-Leclercq

Affiliation Pharmacognosy Research Group, Louvain Drug Research Institute, Université Catholique de Louvain, Brussels, Belgium

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Abstract

Malaria is a major parasitic disease and is responsible for almost one million deaths each year in Africa. There is an urgent need to discover new active compounds. Nature and particularly plants are a potential source of new antimalarial drugs since they contain a quantity of metabolites with a great variety of structures and pharmacological activities. This review covers the compounds with antiplasmodial activity isolated from plants which have been published during 2009 organized according to their phytochemical classes. Details are given for substances with IC_{50} values ≤ 11 µM. Sixty-seven references are identified.

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Introduction

There were an estimated 247 million malaria cases among 3.3 billion people at risk in 2006, causing nearly a million deaths, mostly of children under 5 years (WHO, 2008). This disease, transmitted by an *Anopheles* mosquito, is caused by *Plasmodium* species. The parasite is now resistant to a number of antimalarials but plants can offer new metabolites with an original mode of action such as artemisinin from *Artemisia annua* which can be active on resistant strains. In this review, all antiplasmodial metabolites new or already known and isolated from plants to treat malaria and published in 2009 are described and organised according to their phytochemical classes. All the activities were determined *in vitro* on *Plasmodium falciparum* strains unless specified and bioguided fractionation was also based on this antimalarial test. Activities were assessed on different strains among which some are chloroquine sensitive (NF54, 3D7, D6, F32, D10, Ghana, TM4), chloroquine resistant (FcB1, W2, FCM29, Dd2, FCR-3) and/or multidrug resistant (K1) strains, to find effective compounds on resistant malaria. We considered that those having an IC_{50} ≤ 11 µM may have some interest for further development, while those with a lower activity were less interesting. That is why we only give structures for these promising compounds, the others are cited in tables. Compounds tested *in vivo* are also cited. We also analysed the phytochemical classes of these metabolites published in 2009 and the families of plant from which they were isolated and compared these data with those of compounds published from 2005 to 2008. Other reviews already exist for compounds published before 2005 [1–7], or before 2009 [8–10].

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Correspondence
Joanne Bero
Pharmacognosy Research Group
Louvain Drug Research Institute
Université Catholique de Louvain
Avenue E. Mounier 72
1200 Brussels
Belgium
Phone: + 32 27 64 72 92
Fax: + 32 27 64 72 93
Joanne.bero@uclouvain.be

Phenolic Derivatives

Flavonoid derivatives (Fig. 1)

The hexane extract of ground fruits of *Neuraputia magnifica* var. *magnifica* (Engl.) Emmerich (Rutaceae) was fractionated to obtain 2′-hydroxy-3,4,4′,5,6′-pentamethoxychalcone (**1**) which exhibited an antiplasmodial activity with an IC_{50} of 6.9 µM on 3D7 [11].

A new *β*-hydroxydihydrochalcone named (*S*)-elatadihydrochalcone (**2**) was isolated from the seedpods of *Tephrosia elata* Deflers. (Leguminosae) and showed antiplasmodial activity with IC_{50} values of 7.9 and 15.5 µM, respectively, on D6 and W2 [12].

A new isoprenylated flavone, artopeden A (**3**) was isolated from the bark of *Artocarpus champeden* Spreng. (Moraceae) and showed antiplasmodial activity with an IC_{50} of 0.11 µM against 3D7 [13].

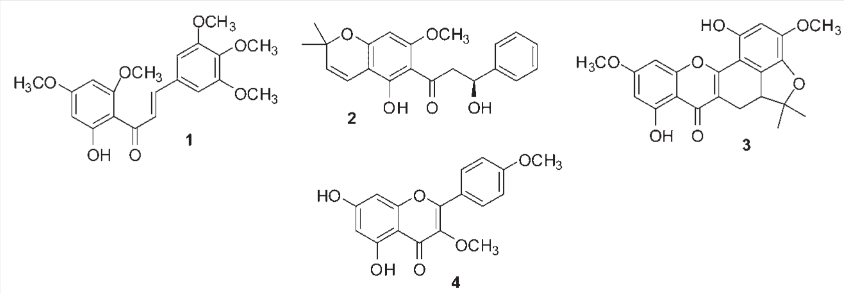

Fig. 1 Flavonoid derivatives with moderate or promising activity *in vitro* against various strains of *Plasmodium falciparum*.

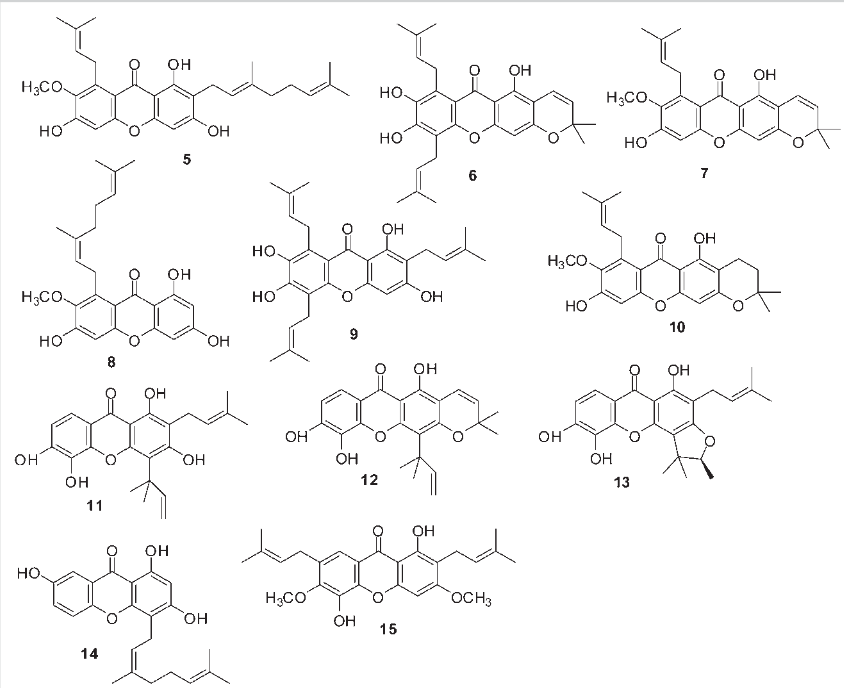

Fig. 2 Xanthones with moderate activity *in vitro* against various strains of *Plasmodium falciparum*.

Baccharis dracunculifolia D.C. (Asteraceae) contains ermanin (**4**) having an IC_{50} of 8.3 µM on D6 and of 7.0 µM on W2 [14].

Xanthones (➲ Fig. 2)

Two new xanthones, butyraxanthones A and B (**5** and **6**), were isolated from the stem bark of *Pentadesma butyracea* Sabine (Clusiaceae), together with four known xanthones: xanthone I (**7**), rubraxanthone (**8**), garcinone E (**9**) and 3-isomangostin (**10**). They exhibited antiplasmodial activity against FcB1 with IC_{50} values of, respectively, 6.3, 5.8, 4.7, 8.3, 6.0 and 7.6 µM but were cytotoxic against a human breast cancer cell line (MCF-7) with IC_{50} values of, respectively, 7.3, 7.1, 9.6, 6.3, 3.2 and 2.9 µM [15].
Three xanthones: gerontoxanthone I (**11**), macluraxanthone (**12**) and formoxanthone C (**13**) were isolated from the stem bark of *Cratoxylum maingayi* Dyer (Clusiaceae) and another one [fuscaxanthone E (**14**)] from the fruits of *Cratoxylum cochinchinense* Blume (Clusiaceae). They displayed antimalarial activity against K1 with IC_{50} values of 4.2, 3.4, 3.0 and 7.9 µM, respectively [16].
A new xanthone, 1,5-dihydroxy-3,6-dimethoxy-2,7-diprenylxanthone (**15**) was obtained from *Garcinia griffithii* T. Anderson (Clusiaceae). It showed antiplasmodial activity with an IC_{50} of 7.3 µM on a Ghana strain [17].

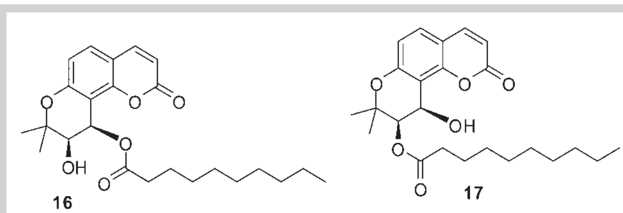

Fig. 3 Coumarins with moderate or promising activity *in vitro* against various strains of *Plasmodium falciparum*.

Coumarins (➲ Fig. 3)

The methanolic extract of the rhizomes of *Angelica purpuraefolia* T.H. Chung (Apiaceae) was investigated and two natural khellactones, (+)-4′-decanoyl-*cis*-khellactone (**16**) and (+)-3′-decanoyl-*cis*-khellactone (**17**) were isolated. These two compounds were evaluated for antiplasmodial activities and showed growth inhibitory activity against D10 with IC_{50} values of 1.5 and 2.4 µM, respectively [18].

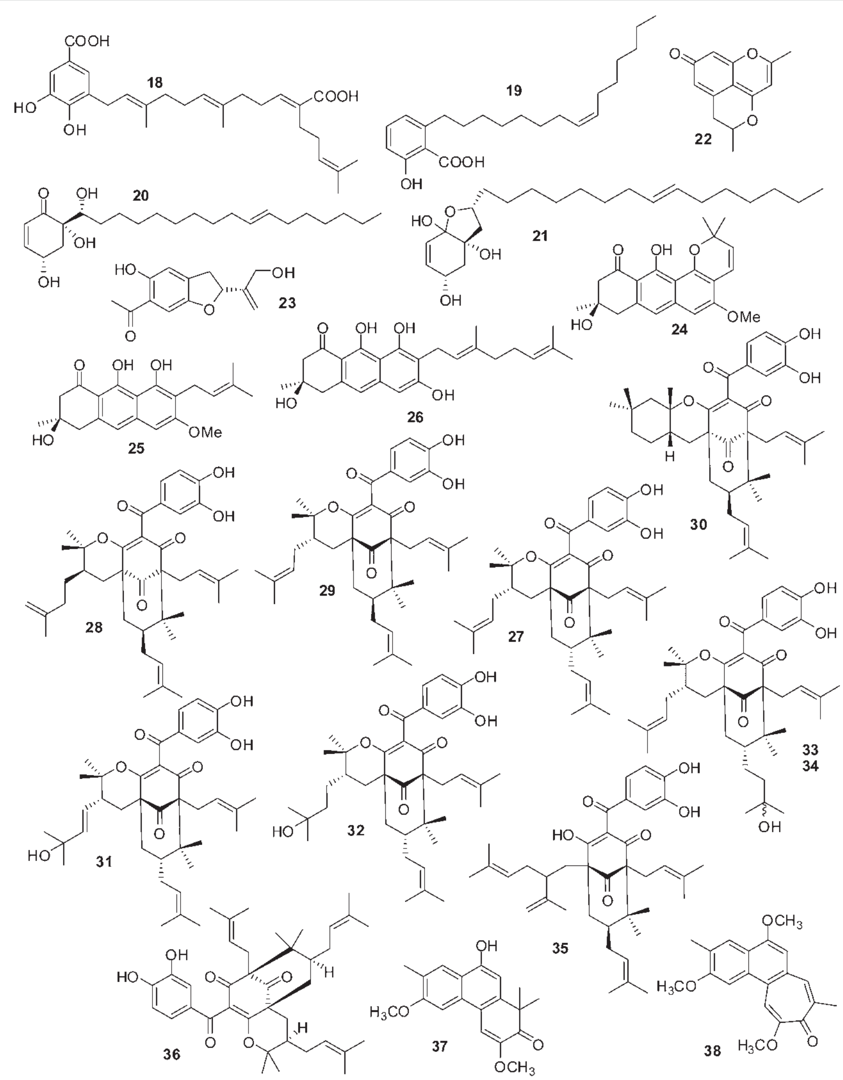

Fig. 4 Other phenolic derivatives with moderate or promising activity *in vitro* against various strains of *Plasmodium falciparum*.

Other phenolic derivatives (Fig. 4)

Compound **18** was isolated from the dichloromethane extracts of the leaves of *Piper heterophyllum* Ruiz & Pav. and *P. aduncum* L. (Piperaceae) and exhibited activity with an IC_{50} of 7.0 µM on F32 [19].

The petroleum ether extract of *Viola websteri* Hemsl. (Violaceae) was investigated and the main antiplasmodial compound was 6-(8′Z-pentadecenyl)-salicylic acid (**19**) with an IC_{50} of 10.1 µM (D10). Given intraperitoneally, **19** showed *in vivo* a 63% suppression of parasitemia in *P. berghei* infected mice treated at 10 mg/kg/day. When used prophylactically a suppression of 70.1% at the same dose was recorded [20, 21].

The bioassay-guided purification of the CH_2Cl_2 extract of the bark of *Tapirira guianensis* Aubl. (Anacardiaceae) led to the isolation of two cyclic alkyl polyol derivatives: 4,6,2′-trihydroxy-6-[10′(*Z*)-heptadecenyl]-1-cyclohexen-2-one (**20**) and 1,4,6-trihydroxy-1,2′-epoxy-6-[10′(*Z*)-heptadecenyl]-2-cyclohexene (**21**). The antiplasmodial activity of a mixture of these two compounds showed an IC_{50} of 4.7 µM on F32 and 5.4 µM on FcB1 [22].

A new chromone, 10,11-dihydroanhydrobarakol (**22**), which showed antiplasmodial activity against 3D7 (IC_{50} = 2.3 µM), was isolated from flowers of *Cassia siamea* Lam. (Caesalpinaceae) [23].

Studies on *Baccharis dracunculifolia* D.C. (Asteraceae) allowed the isolation of viscidone (**23**) which showed an IC_{50} of 8.1 µM on D6 and of 9.8 µM on W2 [14].

Three phenolic compounds, vismione B (**24**), F (**25**) and E (**26**) were isolated from the fruits of *Cratoxylum cochinchinense* Blume (Clusiaceae) and displayed antimalarial activity against K1 with IC_{50} values of 1.86, 4.76 and 10.97 µM, respectively [16].

Acyl phloroglucinols [isogarcinol (**27**), cycloxanthochymol (**28**), 7-epi-isogarcinol (**29**), coccinone A (**30**), B (**31**), C (**32**), D (**33**) and E (**34**), and 7-epi-garcinol (**35**)] from *Moronobea coccinea* Aubl. (Clusiaceae) exhibited an activity with IC_{50} values of 3.5, 2.1, 5.1, 4.3, 5.5, 9.0, 7.0, 4.9 and 10.1 µM, respectively, on FcB1 [24].

Isoxanthochymol (**36**) was obtained from *Garcinia griffithii* T. Anderson (Clusiaceae) and showed antiplasmodial activity with an IC_{50} of 4.5 µM on a Ghana strain but it was also cytotoxic against MRC-5 cells (IC_{50} = 7.5 µM) [17].

A new phenanthrenone, 9-*O*-demethyltrigonostemone (**37**), and a new phenanthropolone (**38**) were isolated from the roots of *Strophioblachia fimbricalyx* Boerl. (Euphorbiaceae) and displayed antiplasmodial activity (IC_{50} values of 8.7 and 9.9 µM, respectively) against K1 [25].

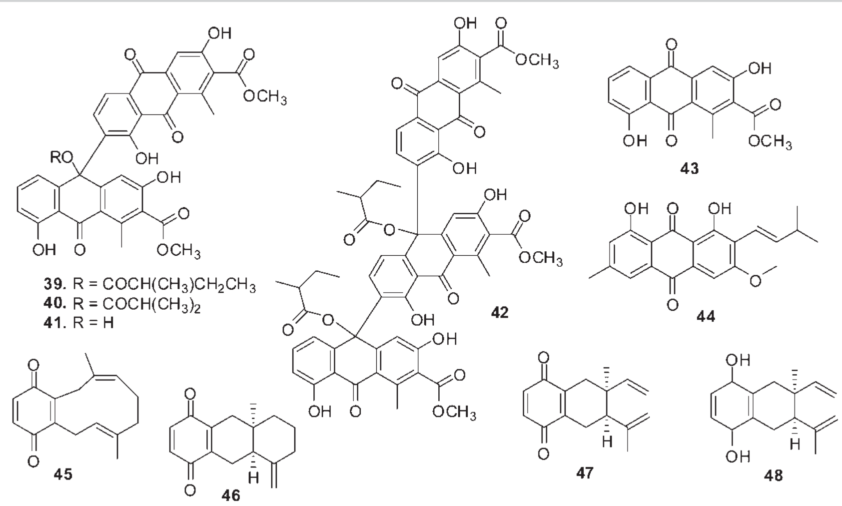

Fig. 5 Quinones and derivatives with moderate or promising activity *in vitro* against various strains of *Plasmodium falciparum*.

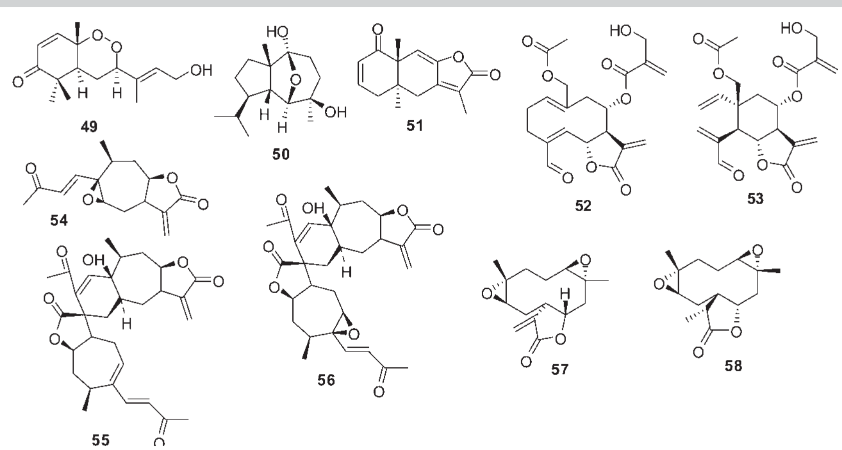

Fig. 6 Sesquiterpenes with moderate or promising activity *in vitro* against various strains of *Plasmodium falciparum*.

Quinones and Derivatives (▶ Fig. 5)

Bioassay-guided fractionation of an ethanol extract of the bark of *Scutia myrtina* Kurz (Rhamnaceae) led to the isolation of three new anthrone–anthraquinones dimers, scutianthraquinones A (**39**), B (**40**) and C (**41**), one new bisanthrone–anthraquinone trimer, scutianthraquinone D (**42**) and the known anthraquinone, aloesaponarin I (**43**). These compounds exhibited antiplasmodial activities with IC_{50} values of 1.23, 1.14, 3.14, 3.68 and 5.58 µM, respectively, on Dd2 and 1.2, 5.4, 15.4, 5.6 and > 50 µM, respectively, on FCM29 [26].

A phytochemical study of the stem bark of *Vismia laurentii* De Wild. (Clusiaceae) resulted in the isolation of a known compound, vismiaquinone A (**44**) which showed antimalarial activity of 1.42 µM against W2 [27].

A new compound named globiferin (**45**) was isolated from root extracts of *Cordia globifera* W.W. Sm. (Boraginaceae) with cordiachrome B (**46**), cordiachrome C (**47**) and cordiaquinol C (**48**). Antimalarial activities (IC_{50}) were 8.7, 6.2, 0.8 and 1.2 µM, respectively, on K1 [28].

Terpenoids

Sesquiterpenes (▶ Fig. 6)

Okundoperoxide (**49**) was isolated by bioassay-guided fractionation from extracts of roots of *Scleria striatonux* de Wild. (Cyperaceae) and possessed IC_{50} values of 1.8, 1.8, 5.6, 4.9 µM, respectively, on W2, D6, K1, NF54 [29].

An antiplasmodial bioguided investigation of the EtOAc extract of the aerial parts of *Teucrium ramosissimum* Desf. (Lamiaceae) led to the isolation of homalomenol C (**50**). Its IC_{50} was 4.7 µM on FcB1 [30].

The ethyl acetate extract of *Siphonochilus aethiopicus* (Schweinf.) B.L. Burtt (Zingiberaceae) rhizomes was fractionated to isolate a novel furanoterpenoid (**51**). This compound showed antiplasmodial activity with IC_{50} values of 13.9 and 7.2 µM, respectively, on D10 and K1 [31].

Bioassay-guided fractionation led to the isolation of two new sesquiterpene lactones (**52** and **53**) from an extract of *Distephanus angulifolius* (DC.) H. Rob. & B. Kahn (Asteraceae). The isolated compounds showed IC_{50} values of 1.9 and 1.55 µM on D10 and 3.24 and 2.10 µM on W2, respectively [32].

Bioactivity-guided fractionation of the dichloromethane extract of *Xanthium brasilicum* Vell. (Asteraceae) resulted in the isolation of three bioactive sesquiterpene lactones: 8-epixanthatin 1*β*,5*β*-epoxide (**54**), and the dimers pungiolide A (**55**) and B (**56**). They showed IC_{50} values of 6.5, 5.0 and 6.5 µM against K1 [33].

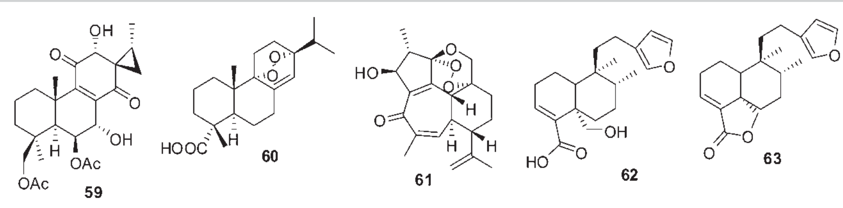

Fig. 7 Diterpenes with moderate activity *in vitro* against various strains of *Plasmodium falciparum.*

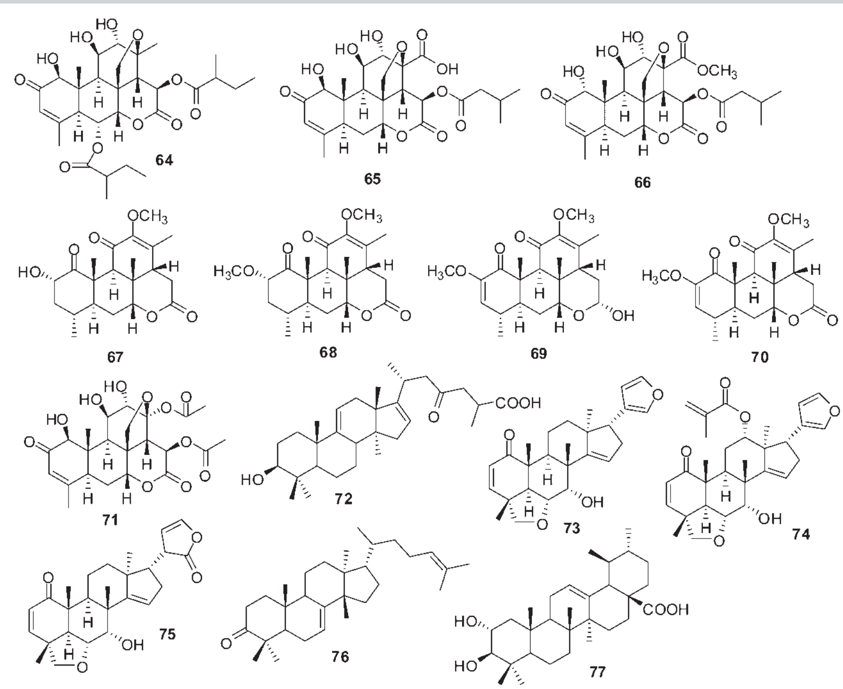

Fig. 8 Triterpenes with moderate or promising activity *in vitro* against various strains of *Plasmodium falciparum.*

Fractionation of the ethyl acetate extract of *Carpesium cernuum* L. (Asteraceae) yielded four characterised sesquiterpenoid lactones among which 11(13)-dehydroivaxillin (**57**) and 11-epi-ivaxillin (**58**) exhibited antiplasmodial activity against D10 with IC_{50} values of 2.0 and 9.3 µM [34].

In vivo antiplasmodial activity of **57** showed a suppression of parasitemia of 58.6% with a dose of 2 mg/kg/day in the four-day test [35].

Diterpenes (▶ Fig. 7)

A new diterpene, 12-*O*-deacetyl-6-*O*-acetyl-19-acetyloxycoleon Q (**59**), and a known one (**60**) were isolated from the aerial parts of *Anisochilus harmandii* Doan (Lamiaceae) and exhibited antiplasmodial activity with IC_{50} values of 6.5 and 9.1 µM on K1 [36].

A known compound, caniojane (**61**), was isolated from the roots of *Jatropha integerrima* Jacq. (Euphorbiaceae) and was evaluated for its antiplasmodial activity: IC_{50} of 9.6 µM against K1 [37].

Baccharis dracunculifolia D.C. (Asteraceae) was shown to contain hautriwaic acid (**62**) and hautriwaic acid lactone (**63**) which had IC_{50} values of 9.0 and 2.5 µM, respectively, on D6 and 7.8 and 7.0 µM, respectively, on W2 [14].

Triterpenes (▶ Fig. 8)

A new quassinoid named simalikalactone E (**64**) was extracted from *Quassia amara* L. (Simaroubaceae) leaves and inhibited *Plasmodium falciparum* with IC_{50} values of 24 nM on W2, 45 nM on FcB1 and 68 nM on F32 [38].

Two new quassinoids, delaumonones A (**65**) and B (**66**) were isolated from the bark of *Laumoniera bruceadelpha* Noot. (Simaroubaceae) and showed an antimalarial activity on 3D7 (IC_{50} = 0.6 and 1.1 µM) [39].

Four other quassinoids were isolated from the dichloromethane extract of *Quassia amara* L. (Simaroubaceae): picrasin B (**67**), H–J (**68**–**70**). These compounds have antimalarial activities with IC_{50} values of, respectively, 0.8, 3.4, 2.6 and 4.2 µM on W2 [40].

Isobrucein B (**71**) isolated from *Picrolemma sprucei* Hook. f. (Simaroubaceae) was tested for its antimalarial activity against the K1 strain (IC_{50} = 2.1 nM) [41].

Garcihombronane D (**72**) was obtained from *Garcinia celebica* L. (Clusiaceae) and showed an activity with an IC_{50} of 7.7 µM on a Ghana strain [17].

Three new limonoids, ceramicines B–D (**73**–**75**), were isolated from the bark of *Chisocheton ceramicus* Miq. (Meliaceae). Ceramicines exhibited an antiplasmodial activity with IC_{50} values of 0.56, 4.8 and 5.1 µM, respectively, on 3D7 [42].

A phytochemical study of the stem bark of *Vismia laurentii* De Wild. (Clusiaceae) resulted in the isolation of a tetracyclic triterpene, tirucalla-7,24-dien-3-one (**76**) which showed antimalarial activity of 1.18 µM against W2 [27].

Baccharis dracunculifolia D.C. (Asteraceae) was shown to contain 2α-hydroxyursolic acid (**77**) which presented an IC_{50} of 6.8 µM on D6 and 6.4 µM on W2 [14].

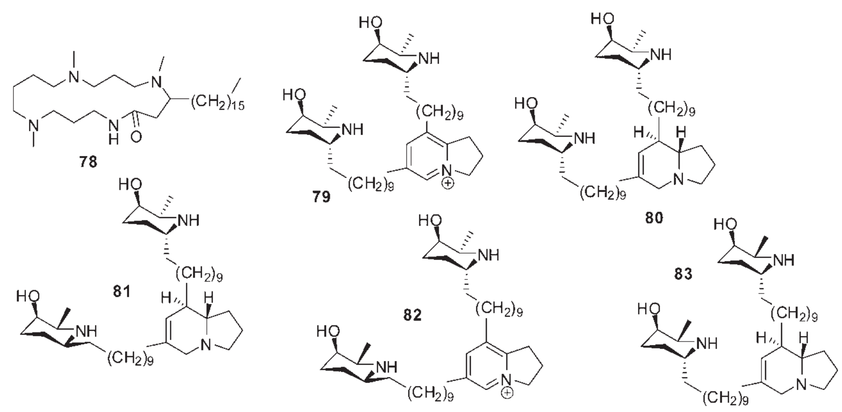

Fig. 9 Ornithine and lysine derivatives with promising activity *in vitro* against various strains of *Plasmodium falciparum*.

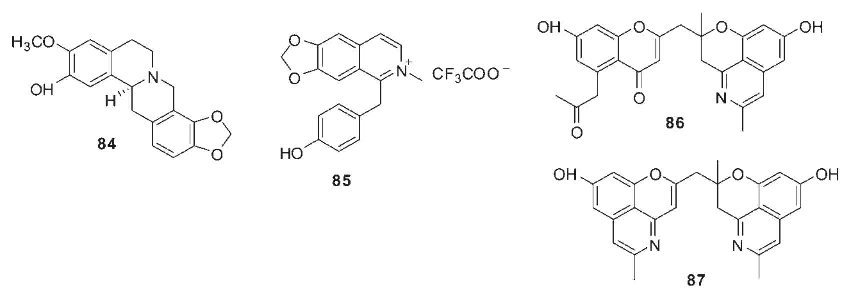

Fig. 10 Phenylalanine and tyrosine derivatives with moderate activity *in vitro* against various strains of *Plasmodium falciparum*.

Alkaloids

Ornithine and lysine derivatives (▶ Fig. 9)

Researches on *Albizia schimperiana* Oliv. (Leguminosae) allowed the isolation of the new bioactive macrocyclic spermine alkaloid, namely 5,14-dimethylbudmunchiamine L1 (**78**). This compound demonstrated antimalarial activity against D6 and W2 with IC_{50} values of 0.27 and 0.34 µM [43].

Four new indolizidines: prosopilosidine (**79**), prosopilosine (**80**), isoprosopilosine (**81**) and isoprosopilosidine (**82**) and a known one, juliprosopine (**83**) were isolated from *Prosopis glandulosa* Torrey var. *glandulosa* (Leguminosae). These compounds exhibited potent activity with IC_{50} values of 62, 191, 132, 67 and 350 nM, respectively, on D6 and 152, 366, 238, 192 and 604 nM, respectively, on W2. Prosopilosine also showed *in vivo* antimalarial activity, exhibiting 48 % suppression of parasitemia at 2 mg/kg/day/i. p. against *Plasmodium berghei* after 3 days of treatment [44].

Phenylalanine and tyrosine derivatives (▶ Fig. 10)

A known alkaloid, cheilanthifoline (**84**), from *Corydalis calliantha* D.G. Long (Papaveraceae) showed antiplasmodial activitiy against TM4 and K1 strains with IC_{50} values of 2.8 and 3.8 µM, respectively [45].

The dichloromethane extract of *Doryphora sassafras* Endl. (Monimiaceae) was fractionated to obtain a quaternary benzylisoquinoline alkaloid, 1-(4-hydroxybenzyl)-6,7-methylenedioxy-2-methylisoquinolinium trifluoroacetate (**85**) which presented an antiplasmodial activity of 4.4 µM on Dd2 and 3.0 µM on 3D7 [46].

Two new dimeric alkaloids, cassiarins D (**86**) and E (**87**), which showed antiplasmodial activity against 3D7 (IC_{50} = 3.6 and 7.3 µM), were isolated from flowers of *Cassia siamea* Lam. (Caesalpinaceae) [23].

Tryptophane derivatives (▶ Fig. 11)

Flinderole A (**88**) was isolated from *Flindersia acuminata* C.T. White (Rutaceae), flinderoles B–C (**89**–**90**) from *F. amboinensis* Poir., and isoborreverine (**91**) and dimethylisoborreverine (**92**) from *F. fournieri* Pancher & Sebert. They have selective antimalarial activities with IC_{50} values of 1.42, 0.15, 0.34, 0.32 and 0.08 µM, respectively, on Dd2 while on cancer cells (HEK-293) their IC_{50} values were 19.97, 2.13, 9.75, 8.99 and 4.09 µM, respectively [47].

Three new alkaloids, alstiphyllanines B–D (**93**–**95**), were isolated from *Alstonia macrophylla* Wall. (Apocynaceae) and showed antiplasmodial activity against 3D7 with IC_{50} values of 0.6, 10.0 and 4.5 µM, respectively [48].

Other N-containing compounds (▶ Fig. 12)

Studies on the CH_2Cl_2/MeOH extract from the roots of the Australian tree *Mitrephora diversifolia* Miq. (Annonaceae) resulted in the purification of the known 5-hydroxy-6-methoxyonychine (**96**) which displayed IC_{50} values of 9.9 and 11.4 µM, respectively, on 3D7 and Dd2 [49].

Other Metabolites (▶ Fig. 13)

The flower extracts of *Goniothalamus laoticus* (Fin. & Gagnep.) Bân (Annonaceae) were fractionated to obtain a styryllactone, (+)-3-acetylaltholactone (**97**). This compound was evaluated for its antiplasmodial activity against K1 (IC_{50} = 9.5 µM) but it showed cytotoxicity against human cancer cell lines with IC_{50} values of 10.6, 3.3 and 6.6 µM, respectively, on KB, BC1 and NCI-H187 [50].

A linear polyacetylenic diol (**98**) was isolated from *Bidens pilosa* L. (Asteraceae), and exhibited antiplasmodial properties *in vitro* with IC_{50} of 1.8 µM on FCR-3 as well as antimalarial activity by in-

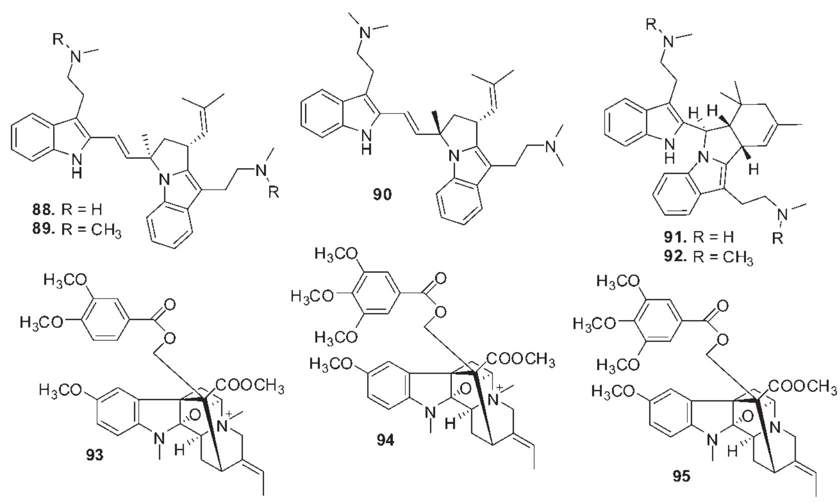

Fig. 11 Tryptophane derivatives with moderate or promising activity *in vitro* against various strains of *Plasmodium falciparum*.

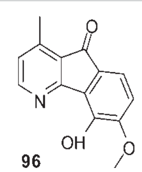

Fig. 12 Other N-containing compounds with moderate activity *in vitro* against various strains of *Plasmodium falciparum*.

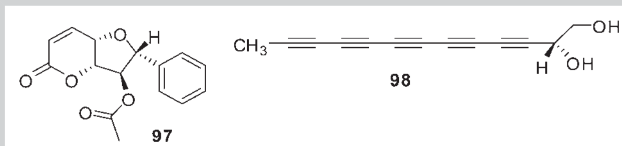

Fig. 13 Other metabolites with moderate or promising activity *in vitro* against various strains of *Plasmodium falciparum*.

travenous injection *in vivo*, which was carried out in mice infected with the *Plasmodium berghei* NK-65 strain. The average parasitemia of 32.8% in the control red blood cells was decreased significantly to 12.1% by the administration of 0.8 mg/kg/day of the compound for four days [51].

Discussion and Conclusions

In traditional medicine, traditional healers use plants for the treatment of malaria or several symptoms of the disease. This review focusing on publications of 2009 shows that some promising new antimalarial compounds can be isolated by the ethnopharmacological and bioguided fractionation approaches. Various extracts of plants were fractionated to obtain 146 compounds which were evaluated for antimalarial activity *in vitro*. Among them, 41 possessed low ($11 < IC_{50} < 50$ µM), 65 moderate ($2 < IC_{50} < 11$ µM) and 31 promising ($IC_{50} < 2$ µM) activity *in vitro* against various strains of *Plasmodium falciparum* which is responsible for the most severe form of malaria. The activity of some of these compounds was tested against various cell lines, normal or cancer cells, but only a few of them for their *in vivo* antimalarial activity. Nevertheless, in these cases, the promising *in vitro* activities could be confirmed by *in vivo* tests. Among them, a phenolic compound: 6-(8′*Z*-pentadecenyl)-salicylic acid, a sesquiterpene lactone: 11(13)-dehydroivaxillin, a tryptophane derivative: prosopilosine, and a linear polyacetylenic diol seem promising.
Moreover, ellagic acid already isolated and tested *in vitro* before 2009 with an IC_{50} of 0.5 µM on D6 and 0.3 µM on W2 with no cytotoxicity, displayed interesting antimalarial efficacy *in vivo* with a parasitemia reduction of 50% at 1.0 mg/kg/day by the intraperitoneal route. This compound could be an interesting candidate for further development [52, 53].

Among the compounds we reviewed, only a few of them exhibited a good activity and should be considered as lead compounds for further investigations (▶ **Table 1**). In 2009, most of the highly active compounds were found in the alkaloid and terpene chemical classes, which was also the case in 2005–2008 (▶ **Fig. 14**). The same trend was observed when considering families from which active compounds were isolated (▶ **Fig. 15**). Most active alkaloids published in 2009 were isolated from the Leguminosae and Rutaceae families [10]. In our previous review, Leguminosae was also identified as a family allowing isolation of a significant number of active alkaloids, while Rutaceae was not found to be particulary interesting although it is a family whose activity is often due to the presence of alkaloids [6].
The more active triterpenes were obtained from Simaroubaceae which seem to have been well studied in 2009 and were not identified as an interesting family in 2005–2008. However, other reviews confirmed that the active antimalarial molecules of the Simaroubaceae are mainly quassinoids [6, 9]. Quassinoids often displayed anticancer activity but the antimalarial activity does not seem to be correlated with the cytotoxicity [54].
When considering highly active compounds and families from which they were isolated and comparing with the results of 2005–2008, we observed that in 2009 no highly active diterpene was isolated, although this class was pointed out to be very interesting in 2005–2008. The same is observed with the Caesalpinaceae family from which they were isolated. This may be explained by the fact that one team focused in 2005–2008 on diterpenes from Caesalpinaceae leading to Kalauni et al. [55] and Linn et al. [56].

Table 1 Tested compounds presenting promising activity with IC_{50} < 2 µM.

Chemical class	Family	Plant	Compound	IC_{50} (µM)
Alkaloids	Rutaceae	*Flindersia acuminata* C. T. White	Flinderole A	1.42 (Dd2)
Akaloids	Rutaceae	*Flindersia amboinensis* Poir.	Flinderole B	0.15 (Dd2)
Alkaloids	Rutaceae	*Flindersia amboinensis* Poir.	Flinderole C	0.34 (Dd2)
Alkaloids	Rutaceae	*Flindersia fournieri* Pancher & Sebert	Isoborreverine	0.32 (Dd2)
Alkaloids	Rutaceae	*Flindersia fournieri* Pancher & Sebert	Dimethylisoborreverine	0.08 (Dd2)
Alkaloids	Apocynaceae	*Alstonia macrophylla* Wall.	Alstiphyllanine B	0.60 (3D7)
Alkaloids	Leguminosae	*Albizia schimperiana* Oliv.	5,14-Dmethylbudmunchiamine L1	0.27 (D6) 0.34 (W2)
Alkaloids	Leguminosae	*Prosopis glandulosa* Torrey	Prosopilosidine	0.06 (D6) 0.15 (W2)
Alkaloids	Leguminosae	*Prosopis glandulosa* Torrey	Prosopilosine	0.19 (D6) 0.37 (W2)
Alkaloids	Leguminosae	*Prosopis glandulosa* Torrey	Isoprosopilosine	0.13 (D6) 0.24 (W2)
Alkaloids	Leguminosae	*Prosopis glandulosa* Torrey	Isoprosopilosidine	0.07 (D6) 0.19 (W2)
Alkaloids	Leguminosae	*Prosopis glandulosa* Torrey	Juliprosopine	0.35 (D6) 0.60 (W2)
Coumarins	Apiaceae	*Angelica purpuraefolia* Chung	(+)-4′-Decanoyl-*cis*-khellactone	1.5 (D10)
Flavonoids	Moraceae	*Artocarpus champeden* Spreng.	Artopeden	0.11 (3D7)
Other metabolites	Asteraceae	*Bidens pilosa* L.	Polyacetylenic diol	1.8 (FCR-3)
Other phenolic derivatives	Clusiaceae	*Cratoxylum cochinchinense* Blume	Vismione B	1.86 (K1)
Quinones	Boraginaceae	*Cordia globifera* W. W. Sm	Cordiachrome C	0.8 (K1)
Quinones	Boraginaceae	*Cordia globifera* W. W. Sm	Cordiaquinol C	1.2 (K1)
Quinones	Rhamnaceae	*Scutia myrtina* Kurz	Scutianthraquinone A	1.23 (Dd2) 1.2 (FCM29)
Quinones	Rhamnaceae	*Scutia myrtina* Kurz	Scutianthraquinone B	1.14 (Dd2) 5.4 (FCM29)
Quinones	Clusiaceae	*Vismia laurentii* De Wild.	Vismiaquinone A	1.42 (W2)
Sesquiterpenes	Cyperaceae	*Scleria striatonux* De Wild.	Okundoperoxide	1.8 (W2) 1.8 (D6) 5.6 (K1) 5.0 (NF54)
Sesquiterpenes	Asteraceae	*Distephanus angulifolius* (DC.) H. Rob. & B. Kahn	(6*S*,7*R*,8*S*)-14-Acetoxy-8-[2-hydroxymethylacrylate]-15-helianga-1(10),4,11(13)-trien-15-al-6,12-olide	1.90 (D10) 3.24 (W2)
Sesquiterpenes	Asteraceae	*Distephanus angulifolius* (DC.) H. Rob. & B. Kahn	(5*R*,6*R*,7*R*,8*S*,10*S*)-14-Acetoxy-8-[2-hydroxymethyl-acrylate]-elema-1,3,11(13)-trien-15-al-6,12-olide	1.55 (D10) 2.10 (W2)
Triterpenes	Simaroubaceae	*Quassia amara* L.	Simalikalactone E	0.02 (W2) 0.05 (FcB1) 0.07 (F32)
Triterpenes	Simaroubaceae	*Quassia amara* L.	Picrasin B	0.80 (W2)
Triterpenes	Meliaceae	*Chisocheton ceramicus* Miq.	Ceramicine B	0.56 (3D7)
Triterpenes	Simaroubaceae	*Laumoniera bruceadelpha* Noot.	Delaumonone A	0.6 (3D7)
Triterpenes	Simaroubaceae	*Laumoniera bruceadelpha* Noot.	Delaumonone B	1.1 (3D7)
Triterpenes	Simaroubaceae	*Picrolemma sprucei* Hook. f.	Isobrucein B	0.002 (K1)
Triterpenes	Clusiaceae	*Vismia laurentii* De Wild.	Tirucalla-7,24-dien-3-one	1.18 (W2)

Three of the most active sesquiterpenes are lactones and were obtained from a plant of the Asteraceae family as it was the case for the "famous" artemisinin.

Among families from which most highly active compounds were isolated in 2005–2008, Menispermaceae and Asphodelaceae are not represented in 2009 while from Moraceae, only one interesting flavonoid (artopeden A) was isolated.

These observations and comparisons show that it is often difficult to assess general rules concerning interesting classes of compounds or interesting families as it may depend highly on the activity of specific research groups. Nevertheless, we can indicate that during 2009, alkaloids from the Leguminosae and Rutaceae families, quassinoids from Simaroubaceae and well-known sesquiterpene lactones from Asteraceae were described as interesting antimalarial compounds with original structures which could be considered as lead compounds for new drugs against resistant malaria.

Supporting information

Tested phenolic derivatives, terpenic compounds, alkaloids and other metabolites presenting low or no activity *in vitro* against various strains of *Plasmodium falciparum* (**Tables 1S–4S**) are available as Supporting Information.

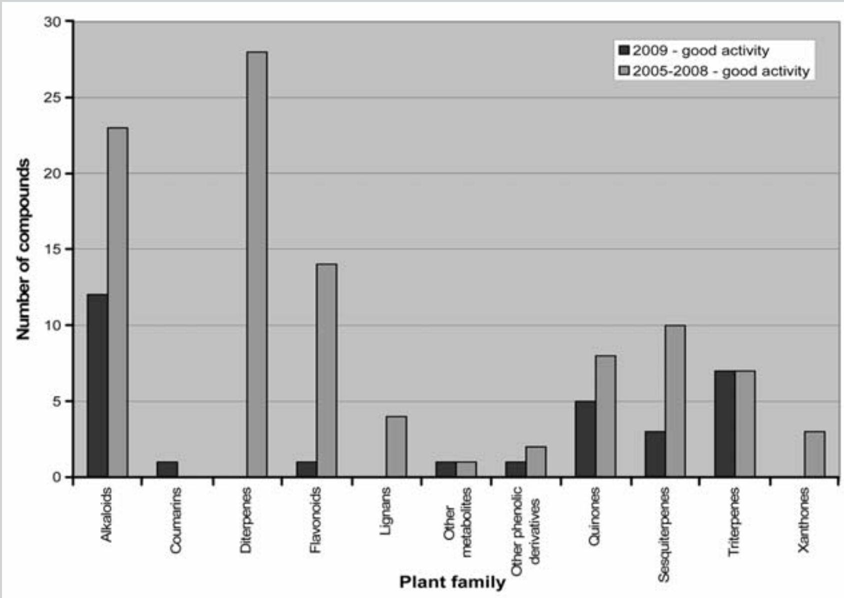

Fig. 14 Number of compounds with good activity (IC_{50} < 2 µM) *in vitro* against various strains of *Plasmodium falciparum*, classified according to their chemical classes.

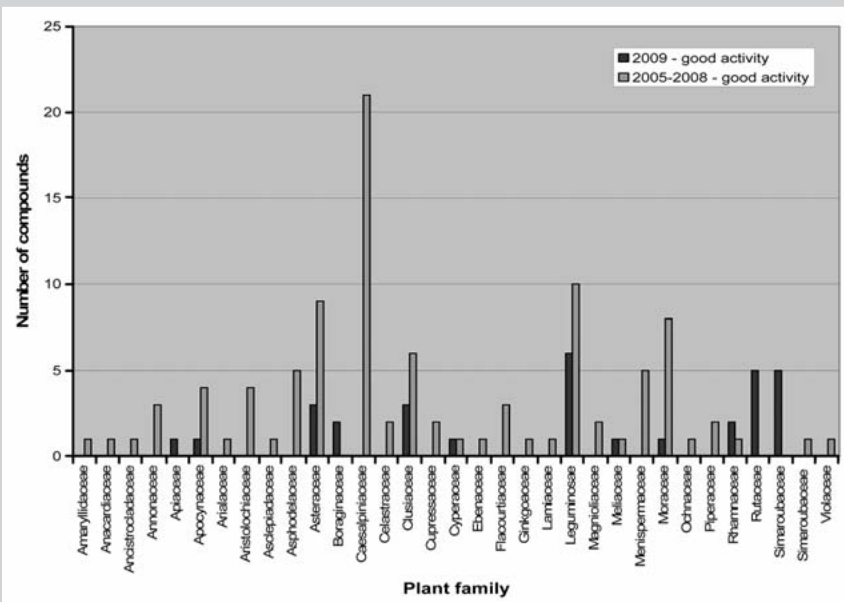

Fig. 15 Number of compounds with good activity (IC_{50} < 2 µM) *in vitro* against various strains of *Plasmodium falciparum*, classified according to the plant family from which they were isolated.

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