**Table S1. Phylogenetic status of medicinal insects (323) and their active pharmaceutical agents**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Evolutionary status | | Insect order | Family | Species | `Representative pharmaceutical agents | | |
| Number/Name | | References/Origin |
| **Apterygota** | | Thysanura | Lepismatidae | *Ctenolepisma villosa* | Unknown | | |
| *Lepisma saccharina* |
| **Pterygota**  **Pterygota**  **Pterygota**  **Pterygota**  **Pterygota**  **Pterygota**  **Pterygota**  **Pterygota**  **Pterygota**  **Pterygota**  **Pterygota**  **Pterygota**  **Pterygota** | **Hemimetabola**  **Hemimetabola**  **Hemimetabola**  **Hemimetabola** | Odonata | Coenagrionidae | *Coenagrion* sp. | amicoumacin B  (LD50: 132 mg/kg mouse, perorally) | | (Thongtan et al., 2002)  endosymbionts |
| Libellulidae | *Crocothemis servilia* |
| *Pantala flavescens* |
| *Sympetrum darwinianum* |
| *S. infuscatum* |
| *Orthetrum melania* |
| Aeschnidae | *Aeschna melanictera* |
| *Anax parthenope julius* |
| Blattaria | Blattidae | *Periplaneta americana* | See the article | | endogenous/ endosymbionts |
| *P. australasiae* |
| *P. fuliginosa* |
| *Blatta orientalis* |
| Blattallidae | *Blattella germanica* |
| *B. latistriga* |
| *Opisthoplata orientalis* |
| Eupolyphaga | *Eupolyphaga sinensis* |
| *E. thibetana* |
| *E. yunnaensis* |
| *E. everestians* |
| *Polyphaga plancyi* |
| Termitidae | *Odontotermes formosanus* | See the article | | endosymbionts |
| *O. hainanensis* |
| *O. foveafrons* |
| *O. annulicornis* |
| *Macrotermes annandalei* |
| *M. barneyi* |
| *M. yunanensis* |
| *M. guangxiensis* |
| *M. longimentis* |
| *M. latinotus* |
| *M. trimorphus* |
| *M. choui* |
| *M. longiceps* |
| *M. menlongensis* |
| *M. jinghongensis* |
| *Globitermes sulphureus* |
| *Hypotermes sumatrensis* |
| Rhinotermitidae | *Coptotermes formosanus* |
| *C. monsetosus menglunensis* |
| *Reticulitermes flaviceps* |
| *R. grandis* |
| *Parrhinotermes khasii* |
| Mantodea | Mantidae | *Paratenodera sinensis* | See the article | | endogenous |
| *P. augustipennis* |
| *Mantis religiosa* |
| *Statilia maculata* |
| *S. nemoralis* |
| *Tenodera sinensis* |
| *T. aridifolia* |
| *T. angustipennis* |
| *Hierodula patellifera* |
| *H. membranacea* |
| Orthoptera | Acrididae | *Oxya chinensis* | hirsutellic acid A (IC50 = 8 µM, *Plasmodium falciparum*) | | (Isaka et al., 2006)  endosymbionts |
| *Acrida lata* |
| *A. cinerea* |
| *Locusta migratoria manilensis* |
| *Ceracris kiangsu* |
| *Patanga japonca* |
| Gryllidae | *Gryllus chinensis* |
| *G. testaceus* |
| *G. mitratus* |
| *Loxoblemmus doenitzi* |
| *Velarifictorus aspersus* |
| *V. micado* |
| Tettigoniidae | *Mecopoda elongata* |
| *Gampsocleis buergeri* |
| Gryllotalpidae | *Gryllotalpa africana* | See the article | | endogenous |
| *G. orientalis* |
| *G. uncspina* |
| Hemiptera | Cicadidae | *Cryptotympana pustulata* | See the article | | endogenous |
| *Cryptotympana atrata* |
| *Cryptotympana mandarina* |
| *Cryptotympana tustulata* |
| *Oncotympana maculaticollis* |
| *Hyalessa ronsnana* |
| *Oncotympana sp.* |
| *Cicadatra shaluensis* |
| *Cicada flammata* |
| *Mogannia conica* |
| *Platypleura kaempferi* |
| *Huechys sanguinea* |
| *H. philamata* |
| *H. thoracica* |
| Pemphigidae | *Schlechtendalia chinensis* | See the article | | aphid parasites |
| *S. peita* |
| *Nurudea sinica* |
| *N. shiraii* |
| *N. rosea* |
| *Kaburagia ensigallis* |
| *K. ovogallis* |
| *K. rushicola* |
| *K. ovatirhusicola* |
| *Meitanaphis elongallis* |
| *M. flavogallis* |
| *M. microgallis* |
| *Floraphis meitanaensis* |
| *F. choui* |
| Coccidae | *Ericerus pela* | See the article | | endogenous |
| Lacciferidae | *Kerria yunnanensis* |
| *K. lacca* |
| *K. chinensis* |
| *K. nepalensis* |
| *K. pusana* |
| *K. ruralis* |
| *K. sindica* |
| *Metatachardin myrica* |
| Fulgoridae | *Lycorma delicatula* | Unknown | | |
| Pentatomidae | *Aspongopus chinensis* | See the article | | endogenous |
| *Tessaratoma papillosa* |
| *T. quadrata* |
| *Cyclopelta parva* |
| Gerridae | *Aquarium paludum* | Unknown | | |
| Belostomatidae | *Lethocerus indicus* | Unknown | | |
| **Holometabola**  **Holometabola**  **Holometabola**  **Holometabola**  **Holometabola**  **Holometabola**  **Holometabola**  **Holometabola** | Coleoptera | Carabidae | *Pheropsophus jessoensis* | Unknown | | |
| Dytiscidae | *Cybister tripunctatus* | Unknown | | |
| *C. japonicus* |
| *C. limbatus* |
| Gyrinidae | *Gyrinus curtus* | Unknown | | |
| Meloidae | *Mylabris phalerata* | See the article | | endogenous |
| *M. cichorii* |
| *M. schonherri* |
| *M. calida pallas* |
| *Epicauta gorhami* |
| *E. ruficeps* |
| *E. aptera* |
| *E. caraganae* |
| *Hycleus cichorii* |
| *Hycleus phaleratus* |
| *Meloe coaretatus* |
| Staphylinidae | *Paederus fuscipes* | See the article | | endosymbionts |
| *P. tamulus* |
| *P. densipennis* |
| *P. parallelus* |
| *P. tibelenus* |
| Elateridae | *Pleonomus canaliculatus* | Unknown | | |
| *Agriotes fuscicollis* |
| *Agriotes sericeus* |
| *Melanotus caudes* |
| *Selatosomus latus* |
| Scarabaeidae | *Catharsius molossus* | N-acetyldopamine dimers  (COX-1: IC50=78.85 µM;COX-2: IC50=6.43µM) | | (Lu et al., 2015)  endogenous/ endosymbionts |
| *Scarabaeus sacar* |
| *Copris ochus* |
| Geotrupidae | *Geotrupes laevistriatus* | Unknown | | |
| *G. substriatellus* |
| Dynastidae | *Allomyrina dichotoma* | dicotastin Allomyrinanoid A | | (Niu et al., 2016)  endogenous |
| *Alissonotum crassum* |
| *Eupatorus hardwicki* |
| Lyctidae | *Lyctus brunneus* | Unknown | | |
| Lampyridae | *Luciola chinensis* | Unknown | | |
| *L. ficta* |
| *L. vitticollis* |
| Melolonthidae | *Holotrichia diomphalia* | 1. holotricin (IC50=2.5 µg/mL, E. coli ATCC2592) 2. elaiophylin | | (Lee et al., 1994; Guo et al, 2015)  endogenous |
| *H. oblila* |
| *H. sauteri* |
| *H. parallela* |
| Rutelidae | *Anomala corpulenta* |
| Cetoniidae | *Oxycetonia jucunda* |
| *Protaetia brevitarsis* |
| Cerambycidae | *Apriona germari* | Unknown | | |
| *Anoplophora chinensis* |
| *Anoplophora glabripennis* |
| *Batocera horsfieldi* |
| Tenebrionidae | *Martianus dermestoides* | rynchopeterines A–E (IC50=7.67-12.3µg/mL, DPPH ) | | (Xiao et al., 2017)  endogenous |
| *Blaps rynchopetera* |
| *Tenebrio molitor* |
| Silphidae | *Nicrophorus sp.* | Unknown | | |
| Curculionidae | *Otidognathus davidi* | Unknown | | |
| *Cyrtotrachelus longimanus* |
| Neuroptera | Myrmeleontidae | *Euroleon sinicus* | Unknown | | |
| *Myrmeleon micans* |
| *Distoleon yunnaus* |
| *Palpares sinicus* |
| *Epicanthaclisis continentalis* |
| *Glenuroides japonicus* |
| Trichoptera | Phrygancidae | *Phryganea japonica* | Unknown | | |
| Lepidoptera | Hepialidae | *Hepialus armoricanus* | See the article | | endosymbionts |
| *H. kangdinensis* |
| *H. baimaensis* |
| *H. yushuensis* |
| *H. oblifurcus* |
| *H. albipictus* |
| *H. menyuanicus* |
| *H. sichuanus* |
| *H. kangdingroides* |
| *H. yunlongensis* |
| *H. lijiangensis* |
| *H. zhangmoensis* |
| *H. zhayuensis* |
| *H. ganna* |
| *H. macilentus* |
| *H. renzhiensis* |
| *H. altaicola* |
| *Palpifer sexnotatus* |
| *P. signifer* |
| *P. excrescens* |
| *P. yunnanensis* |
| *P. anhuiensis* |
| *P. xizangensis* |
| *P. jingdongensis* |
| *P. giganodus* |
| *P. fujianodus* |
| *P. nodus* |
| *P. miniatus* |
| *P. regius* |
| *Hepialiscus nepalensis* |
| *Hepialiscus sylvinus* |
| *Hepialiscus flavus* |
| *Forkalus xizangensis* |
| *Bipectilus yunnanensis* |
| *Napialus hunanensis* |
| *Thitarodes zhangmoensis* |
| *Thitarodes xiaojinensis* |
| Eucleidae | *Cnidocampa flavescens* | Unknown | | |
| *Thosea sinensis* |
| *T. grandis* |
| *T. sythoffi* |
| *T. loesa* |
| Pyralidae | *Ostrinia furnacalis* | Unknown | | |
| *Procera venoosatum* |
| *Aglossa dimidiate* |
| *Herculia glaucinalis* |
| *Hydrillodes morosa* |
| *H. repugnalis* |
| *Nodaria niphona* |
| *Ostrinia nubilalis* |
| Noctuidae | *Hydrillodes morosa* | Unknown | | |
| *Nodaria niphona* |
| *Agrotis ypsilon* |
| Arctiidae | *Arctia caja* | Unknown | | |
| Brahmaeidae | *Brahmophthalma japonica* | Unknown | | |
| Psychidae | *Cryptothelea formosicola* | Unknown | | |
| Saturniidae | *Philosmia cynthia ricinia* | See the article | | endogenous |
| *Antheraea pernyi* |
| Bombycidae | *Bombyx mori* | See the article | | endogenous |
| Geometridae | *Biston robustum* | Unknown | | |
| *Biston marginata* |
| Notodontidae | *Phalera bucephala* | Unknown | | |
| *P. assimilis* |
| *Leucodonata bicoloria* |
| *Notodonata dembowskii* |
| Sphingidae | *Smerinthus planus* | Unknown | | |
| *Clanis bilineata* |
| *C. deucalion* |
| Xyloryctidae | *Linoclostis gonatias* | Unknown | | |
| Pieridae | *Pieris brassicae* | Unknown | | |
| *Pieris rapae* |
| *Catopsilia crocalc* |
| Papilionidae | *Pailio machaon* | Unknown | | |
| *P. xuthus* |
| Diptera | Tabanidae | *Hermetia illucens* | See the article | endogenous | |
| *Tabanus pleskei* |
| *T. atratus* |
| *T. bivittatus* |
| *T. buddha* |
| *T. chrysarus* |
| *T. mandarinus* |
| *T. pleskei* |
| *T. trigonus* |
| *T. kiangsuensis* |
| *Atylotus rusticus* |
| *A. bivittateinus* |
| Calliphoridae | *Lucilia sericata* | See the article | endogenous | |
| *Chrysomya megacephala* |
| Hymenoptera | Scoliidae | *Scolia vittifornis* | Venomic protein   1. mastoparan (IC50 = 10 µM, inositol phosphate) 2. phospholipase (PLA1 and PLA2) 3. kinins | (Yokokawa et al., 1989;Nakahata et al., 1990; Mendes and Palma, 2006;Monteiro et al., 2009)  endogenous | |
| *Campsomeris annulata* |
| Xylocopidae | *Platynopoda magnifica* |
| *Xylocopa sinensis* |
| *X. appendiculata* |
| Eumenidae | *Eumenes mediterraneus* |
| *E. pomiformis* |
| Polistidae | *Polistes jokahamae* |
| *P. chinensis* |
| *P. antennalis* |
| *P. japonicus* |
| *P. olivaceus* |
| *P. mandarinus* |
| Polybiidae | *Parapolybia varia varia* |
| Vespidae | *Orancistrocerus drewseni* |
| *Vespa nigrithorax* |
| *V. ducalis* |
| *V. analisparalleia* |
| *V. basalis* |
| *V. binghami* |
| *V. bicolor* |
| *V. affinis* |
| *V. crabro crabro* |
| *V. magnifica* |
| *V. mandarinia* |
| *V. simillima* |
| *V. tropica leefmansi* |
| *Protopolybia exigua* |
| *Polybia occidentalis* |
| Formicidae | *Polyrhachis lamellidens* | See the article | endogenous | |
| *P. vicina* |
| *P. dives* |
| *P. paracamponota* |
| *P. furcata* |
| *P. rastellata* |
| *P. bihamata* |
| *Formica fusca* |
| *F. sanguinea* |
| *F. rufa* |
| *F. approximans* |
| *F. yessensis* |
| *Tetramorium bicarinatum* |
| *Oecophylla smaragdina* |
| *Odontoponera transversa* |
| *Bothroponera rufipes* |
| *Phidologiton offinis* |
| *Tetramorium guineense* |
| *Camponotus japonicus* |
| Apidae | *Apis mellifera caucasica* | See the article | endogenous | |
| *A. florea* |
| *A. andreniformis* |
| *A. laboriosa* |
| *A. cerana* |
| *A. dorsata* |
| *A. mellifera* |
| Cynipidae | *Cynips gallaetinctoriae* | See the article | wasp parasites | |

Note: The insect species marked with yellow color denotes that this insect has been explored for their active pharmaceutical agents during the past decades.

**References**

1. Guo, Z.K., Liu, S.B., Ma, S., and Wang, R. (2015). Antibacterial Metabolites from the Mycelia of the Cockchafer-Derived Streptomyces sp. BCa1. *Chin J Trop Crop* 36**,** 1307-1311.
2. Isaka, M., Kittakoop, P., Kirtikara, K., Hywel-Jones, N.L., and Thebtaranonth, Y. (2005). Bioactive substances from insect pathogenic fungi. *Acc Chem Res* 38**,** 813-823.
3. Lee, S.Y., Moon, H.J., Kurata, S., Kurama, T., Natori, S., and Lee, B.L. (1994). Purification and molecular cloning of cDNA for an inducible antibacterial protein of larvae of a coleopteran insect, Holotrichia diomphalia. *J Biochem* 115**,** 82-86.
4. Lu, J., Sun, Q., Tu, Z.C., Lv, Q., Shui, P.X., and Cheng, Y.X. (2015). Identification of N-Acetyldopamine Dimers from the Dung Beetle Catharsius molossus and Their COX-1 and COX-2 Inhibitory Activities. *Molecules* 20**,** 15589-15596.
5. Monteiro, M.C., Romao, P.R., and Soares, A.M. (2009). Pharmacological perspectives of wasp venom. *Protein Pept Lett* 16**,** 944-952.
6. Nakahata, N., Abe, M.T., Matsuoka, I., and Nakanishi, H. (1990). Mastoparan inhibits phosphoinositide hydrolysis via pertussis toxin-insensitive [corrected] G-protein in human astrocytoma cells. *FEBS Lett* 260**,** 91-94.
7. Niu, L., Gao, J., Li, H., Liu, J., and Yin, W. (2016). Novel skeleton compound Allomyrinanoid A and two purine alkaloids from the adult of Allomyrina dichotoma L. *Bioorg Med Chem Lett* 26**,** 366-369.
8. Thongtan, J., Saenboonrueng, J., Rachtawee, P., and Isaka, M. (2006). An antimalarial tetrapeptide from the entomopathogenic fungus Hirsutella sp. BCC 1528. *J Nat Prod* 69**,** 713-714.
9. Xiao, H., Yin, T.P., Dong, J.W., Wu, X.M., Luo, Q., Luo, J.R., Cai, L., and Ding, Z.T. (2017). Five New Phenolic Compounds with Antioxidant Activities from the Medicinal Insect Blaps rynchopetera. *Molecules* 22.