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Research Article

ADMET-Evaluation, Pharmacokinetics, Drug-likeness and Medicinal Chemistry of GCMS Identified Bioactive Compounds of *Moringa oleifera* Natural-Ripened-Dried Methanolic Pod Extract (MOMPE) as a Potential Source of Natural Drug Frontrunner for Next Generation Drug Design, Development and Therapeutics

Kandeepan C.[1], Suganandam K.[2], Jeevalatha A.[3], Kavitha N.[4], Senthilkumar N.[5], Sutha S.[6], Mohamed Ali Seyed[7], Sanyam Gandhi[8], Ramya S.[9], Grace Lydial Pushpalatha G[10], Abraham GC.[11], King Immanuel J.[12], Jayakumararaj R.[13]*

[1] *PG & Research Department of Zoology, Arulmigu Palaniandavar College of Arts & Culture, Palani – 624601, TN, India*
[2] *Department of Chemistry, Velammal College of Engineering and Technology, Viraganoor, Madurai-625009, TN, India*
[3] *Department of Zoology, GTN Arts College, Dindigul - 624005, TN, India*
[4] *PG & Research Department of Chemistry, Arulmigu Palaniandavar College of Arts & Culture, Palani – 624601, TN, India*
[5] *Institute of Forest Genetics & Tree Breeding* (IFGTB), *Indian Council of Forestry Research & Education (ICFRE), Coimbatore – 641002, TN, India*
[6] *Department of Medicinal Botany, Govt. Siddha Medical College, Palayamkottai, Tamil Nadu, India*
[7] *Department of Biochemistry, Faculty of Science, University of Tabuk, Tabuk, 47731, Kingdom of Saudi Arabia*
[8] *Regulatory Affairs, Takeda Pharmaceuticals, Boston, MA, 02139, USA*
[9] *PG Department of Zoology, Yadava College (Men), Thiruppalai - 625014, Madurai, TN, India*
[10] *PG Department of Botany, Sri Meenakshi Government Arts College, Madurai – 625002, TN, India*
[11] *PG & Research Department of Botany, The American College, Madurai – 625002, TamilNadu, India*
[12] *Department of Zoology, Government Arts College, Melur – 625106, Madurai District, TN, India*
[13] *Department of Botany, Government Arts College, Melur – 625106, Madurai District, TN, India*

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*Address for Correspondence:

Dr. R. Jayakumararaj, *Department of Botany, Government Arts College, Melur – 625106, Madurai District, TN, India*

Abstract

Over centuries, *Moringa oleifera* has been used as an integral part of Ayurveda, Siddha and Unani systems of medicine, besides this miracle tree has a wide range of nutritional and bioactive compounds, including proteins, essential amino acids, carbohydrates, lipids, fiber, vitamins, minerals, phenolic compounds, phytosterols and others. The miracle tree is endowed with a wide range of pharmacological properties, including anti-diabetic, anti-inflammatory, anti-carcinogenic, antioxidant, cardioprotective, antimicrobial and hepatoprotective activities. However, deeper dimensions of authentic data on plant based natural products in relation to drug discovery, pharmacokinetics properties of biomolecules is far lacking. ADMET prospecting is eventually expected to contribute to success of MO based lead candidates in drug design, development program besides saving time and money. This study is the first of its kind reporting summative ADMET (Absorption, Distribution, Metabolism, Excretion and Toxicology) properties of all bioactive compounds *Moringa oleifera* methanolic pod extract (MOMPE) as a potential source of natural drug lead using Swiss ADME. A total of 12 compounds namely - 7-Octadecyne, 2-methyl- ($C_{19}H_{36}$); 3,7,11,15-Tetramethyl-2-hexadecen-1-ol ($C_{20}H_{40}O$); 3,7,11,15-Tetramethyl-2-hexadecen-1-ol ($C_{20}H_{40}O$); 6,9,12,15-Docosatetraenoic acid, me ($C_{23}H_{38}O_2$); Cyclohexanol, 5-methyl-2-(1-methylethyl)- ($C_{10}H_{20}O$); 3,7,11,15-Tetramethyl-2-hexadecen-1-ol ($C_{20}H_{40}O$); Palmitic acid vinyl ester ($C_{18}H_{34}O_2$); .γ.-Tocopherol ($C_{28}H_{48}O_2$); Vitamin E ($C_{29}H_{50}O_2$); Cholesta-7,9(11)-dien-3-ol, 4,4-dim ($C_{29}H_{48}O$); γ.-Sitosterol ($C_{29}H_{50}O$); Stigmasta-5,24(28)-dien-3-ol, (3.β.,24Z)- ($C_{29}H_{48}O$). Most of the MOPBNPs are non-substrate for both P-gp (P-glycoprotein) and CYP (Cytochrome P-450 isoenzymes). All the compounds were evaluated for properties viz., GI absorption, BBB permeant, Pgp substrate, CYP1A2, CYP2C19, CYP2C9, CYP2D6, CYP3A4 inhibitors, Lipinski, Ghose, Veber, Egan, Muegge, rule and Bioavailability Score to provide baseline information on PBNPs in MONRD pod.

Keywords: PBNPs; NGDDT; ADMET; *Moringa oleifera*; Secondary Metabolites MONRD pod

INTRODUCTION

Moringa oleifera has been used as a medicine in India since the 18th century BC[1,2]. Traditional healers used different parts of the plant as traditional medicines[3,4]. The medicinal uses are numerous and have long been recognized as an Ayurvedic[2,5,6], Siddha[7] Unani[2], and various other indigenous systems of medicine. Almost all parts of the plant: root, bark, gum, leaf, fruit (pods), flowers, seeds and seed oil, have been used to treat various diseases, like skin infections, swelling, anemia, asthma, bronchitis, diarrhoea, headache, joint pain, rheumatism, gout, diarrhoea, heart problems, fevers, digestive

disorders, wounds, diabetes, conjunctivitis, hemorrhoids, goiter, earache, measles and smallpox in the indigenous system of medicine[8-14].

Absorption, Metabolism and Excretion of biomolecules from MO

M. oleifera has been regarded as the miraculous tree called 'tree of life' due to its immense nutritional benefits[15]. MO has been best studied for its nutritional benefits[16]. Despite noteworthy content of iron, several studies have found that *M. oleifera* plants have low iron bioavailability[17]. High polyphenolic contents of *M. oleifera* may exhibit a conflicting inhibitory effect on iron absorption via formation of non-bioavailable polyphenol-iron complexes[18]. However, formation of inhibitory complexes that lead to poor iron absorption into the body relies specifically on the structures of polyphenol compounds. In addition, it has suggested that low iron bioavailability due to high phytic acid content; removal of phytic acid may improve bioavailability[18]. Similarly, *M. oleifera* is rich in minerals and vitamins, MO has high calcium content, but presence of oxalic acid in leaves interfere with calcium absorption[19]. MO leaves contain oxalate, which has been suggested as cause of reduced calcium bioavailability. Bioavailability effects caused by the presence of phytic and oxalic acid in dietary consumption have ironically labeled them as anti-nutritional factors. Vit-A, Vit-B are the most significant among reported nutrients from *M. oleifera* leaves and the most abundant natural sources for β-carotene and pro-vitamin A carotenoid. *In vivo* and *in vitro* studies indicate that natural vitamin from *M. oleifera* are readily bioavailable with good absorption of nutritional values. *M. oleifera* include all essential amino acids amenable to efficient absorption of high protein content. Studies suggest that amino acids or proteins in *M. oleifera* are highly digestible that equates to its bioavailability[20].

Toxicology and Safety aspects of biomolecules from MO

Toxicity and safety assessment of *M. oleifera* has been described in many studies, with no significant adverse effects of its consumption based on human studies have been reported. Most of the in vitro studies involved the use of normal human cell lines and cancerous cell lines as the indices for the safety and toxicity of *M. oleifera* extract treatment[21]. Cytotoxicity assessment of aqueous seed extract of *M. oleifera* indicated that 2000 mg/kg dose of administration in mice, no systemic toxicity was observed with no significant changes[22,23] in erythrocytes, platelets, hemoglobin, and hematocrit observed for the control group[24]. Acute toxicity/ LD_{50} of 70% ethanolic *M. oleifera* leaf extracts injected intraperitoneally with 150 mg/mL of extracts at interval 5 min until mortality was reached indicated that lethal dose for AT was 6616.67 mg/kg for rats and 26,043.67 mg/kg for rabbits[25] confirmed by histopathology observation concluded that ethanolic extracts of *M. oleifera* leaves have minimum toxicity if given within appropriate doses and ranges of time.

Blood samples was collected for biochemical analysis of acute oral toxicity of aqueous-methanolic leaf extract on female rats as biomarkers of liver dysfunction found that, at a 2000 mg/kg oral dose, levels of aspartate aminotransferase (AST) increased significantly, total bilirubin and a non-significant decrease in the levels of alanine aminotransferase (ALT) as compared to control. In addition, postmortem analysis showed a non-significant increase in hepatic index (liver to body weight ratio) with mild distortions in liver cells[18]. Studies on AST, ALT and ALP with both seed and leaf extracts of MO indicated that both are safe for consumption in appropriate doses with enhanced immunity and offer hepatoprotective potential[26].

Recent review by Azlan et al[18] highlights that clinical trials performed on humans are essential to investigate behavioral, medical or surgical intervention of targeted properties of biomolecules. Literature data on *M. oleifera*-related clinical trials showed that there are approximately 25 interventional studies that have been registered under registry of clinical trials, of which 15 have been completed, and 10 on-going. Likewise, among the trials, 17 are supplementation diets of *Moringa*, 6 drug interventions, and 2 are *Moringa*-based mouthwashes for orthodontic application[18].

MATERIAL AND METHODS

In silico Drug-Likeliness and Bioactivity Prediction

Drug likeliness and bioactivity of selected molecule was analyzed using the Molinspiration server (http://www.molinspiration.com). Molinspiration tool is cheminformatics software that provides molecular properties as well as bioactivity prediction of compounds[27]. In this analysis, there are two important factors, viz., lipophilicity level (log P) and polar surface area (PSA) directly associated with pharmacokinetic properties (PK) of compounds[9]. In Molinspiration-based bioactivity analysis, the calculation of the bioactivity score of compounds toward GPCR ligands, ion channel modulators, kinase inhibitors, nuclear receptor ligands, protease inhibitors, and other enzyme targets were analyzed by Bayesian statistics. This was carried out for G protein-coupled receptors (GPCR), ion channels, kinases, nuclear hormone receptors, proteases.

In silico ADMET Analysis

SwissADME is a web tool that gives free access to a pool of fast yet robust predictive models for physicochemical properties, pharmacokinetics, druglikeness and medicinal chemistry friendliness, among which in-house proficient methods such as iLOGP (a physics-based model for lipophilicity) or BOILED-Egg (graphical classification model for gastrointestinal absorption and brain access). Further, it enables ADME-related calculation for multiple molecules, allowing chemical library analysis and efficient lead optimization[28]. PK properties, such as Absorption, Distribution, Metabolism, Excretion, and Toxicity (ADMET), of fatty acids were predicted using admerSAR v2.0 server (http://lmmd.ecust.edu.cn/admetsar2/) and the admerSAR server is an open-source computational tool for prediction of ADMET properties of compounds, which makes it a practical platform for drug discovery and other pharmacological research[29,30].

In ADMET analysis, absorption (A) of good drugs depends on factors such as membrane permeability[31] [designated by colon cancer cell line (Caco-2)], human intestinal absorption (HIA)[32], and status of either P-glycoprotein substrate or inhibitor[33]. Distribution (D) of drugs mainly depends on the ability to cross blood-brain barrier (BBB)[34]. The metabolism (M) of drugs is calculated by the CYP, MATE1, and OATP1B1-OATP1B3 models[35]. Excretion (E) of drugs is estimated based on the renal OCT substrate. Toxicity (T) of drugs is predicted on Human Ether-A-Go-Go related gene inhibition, carcinogenic status, mutagenic status, and acute oral toxicity[36]. Pharmacokinetic prediction comprised of solubility (logS), partition coefficient (clogP), drug likeness and molecular weight properties[37]. The drug score was calculated by combining with drug likeness, cLogP, logS, molecular weight and toxicity risks in one handy value than may be used to judge the compound's overall potential to qualify for a drug. https://www.organic-chemistry.org/prog/peo/

RESULTS AND DISCUSSION

Previous studies[38-49] indicates that the successful exploitation of plant based natural products depends on the identification, isolation, purification and ADMET characterization followed by clinical trials before its launch in the market. Phytochemical screening and GCMS analysis revealed the presence of 12 compounds namely - 7-Octadecyne, 2-methyl- ($C_{19}H_{36}$); 3,7,11,15-Tetramethyl-2-hexadecen-1-ol ($C_{20}H_{40}O$); 3,7,11,15-Tetramethyl-2-hexadecen-1-ol ($C_{20}H_{40}O$); 6,9,12,15-Docosatetraenoic acid, me ($C_{23}H_{38}O_2$); Cyclohexanol, 5-methyl-2-(1-methylethyl)- ($C_{10}H_{20}O$); 3,7,11,15-Tetramethyl-2-hexadecen-1-ol ($C_{20}H_{40}O$); Palmitic acid vinyl ester ($C_{18}H_{34}O_2$); .gamma.-Tocopherol ($C_{28}H_{48}O_2$); Vitamin E ($C_{29}H_{50}O_2$); Cholesta-7,9(11)-dien-3-ol, 4,4-dim ($C_{29}H_{48}O$); gamma.-Sitosterol ($C_{29}H_{50}O$); Stigmasta-5,24(28)-dien-3-ol, (3.beta.,24Z)- ($C_{29}H_{48}O$).[14]

ADMET informatics of 7-Octadecyne, 2-methyl- (M1)

MW of M1 = 264.49; # Heavy atoms in M1 = 19; # aromatic Heavy atoms in M1 = 0; Fraction Csp3 in M1 = 0.89; # rotatable bonds in M1 = 12; # H-bond acceptors in M1 = 0; # H-bond donors in M1 = 0; Molar refractivity in M1 = 91.61; Topological polar surface area of M1 = 0; Log Po/w value for M1 = 5.25; The octanol–water partition coefficient (XLOGP3) for M1 = 9.04; lipophilicity of large molecules (WLOGP) for M1 = 6.82; Moriguchi octanol-water partition coefficient (MLOGP) for M1 = 7.01; Silicos-IT Log P in M1 = 7.04; Consensus Log P in M1 = 7.03; ESOL Log S in M1 = -6.38; ESOL Solubility (mg/ml) for M1 = 1.09E-04; ESOL Solubility (mol/l) for M1 = 4.14E-07; ESOL Class value for M1 = PS; Ali Log S in M1 = -8.93; Ali Solubility (mg/ml) for M1 = 3.09E-07; Ali Solubility (mol/l) for M1 = 1.17E-09; Ali Class value for M1 = PS; Silicos-IT LogSw in M1 = -6.44; Silicos-IT Solubility (mg/ml) for M1 = 9.67E-05; Silicos-IT Solubility (mol/l) for M1 = 3.66E-07; Silicos-IT class value for M1 = PS; GI absorption by M1 = Low; BBB permeant in M1 = No; Pgp substrate in M1 = No; CYP1A2 inhibitor - M1 = Yes; CYP2C19 inhibitor - M1 = No; CYP2C9 inhibitor - M1 = No; CYP2D6 inhibitor - M1 = No; CYP3A4 inhibitor - M1 = No; log Kp (cm/s) for M1 = -1.49; Lipinski's Rule violations by M1 = 1; Ghose's Rule violations by M1 = 1; Veber's Rule violations by M1 = 1; Egan's Rule violations by M1 = 1; Muegge's Rule violations by M1 = 2; PAINS # alerts for M1 = 0; Brenk # alerts for M1 = 1; Leadlikeness violations by M1 = 2; SA Score in M1 = 4.83; Bioavailability Score in M1 = 0.55 (Fig.1a; Table 2-6).

ADMET informatics of 3,7,11,15-Tetramethyl-2-hexadecen-1-ol (M2)

MW of M2 = 296.53; # Heavy atoms in M2 = 21; # aromatic Heavy atoms in M2 = 0; Fraction Csp3 in M2 = 0.9; # rotatable bonds in M2 = 13; # H-bond acceptors in M2 = 1; # H-bond donors in M2 = 1; Molar refractivity in M2 = 98.94; Topological polar surface area of M2 = 20.23; Log Po/w value for M2 = 4.66; The octanol–water partition coefficient (XLOGP3) for M2 = 8.19; lipophilicity of large molecules (WLOGP) for M2 = 6.36; Moriguchi octanol-water partition coefficient (MLOGP) for M2 = 5.25; Silicos-IT Log P in M2 = 6.57; Consensus Log P in M2 = 6.21; ESOL Log S in M2 = -5.98; ESOL Solubility (mg/ml) for M2 = 3.10E-04; ESOL Solubility (mol/l) for M2 = 1.05E-06; ESOL Class value for M2 = MS; Ali Log S in M2 = -8.47; Ali Solubility (mg/ml) for M2 = 9.94E-07; Ali Solubility (mol/l) for M2 = 3.35E-09; Ali Class value for M2 = PS; Silicos-IT LogSw in M2 = -5.51; Silicos-IT Solubility (mg/ml) for M2 = 9.06E-04; Silicos-IT Solubility (mol/l) for M2 = 3.05E-06; Silicos-IT class value for M2 = MS; GI absorption by M2 = Low; BBB permeant in M2 = No; Pgp substrate in M2 = Yes; CYP1A2 inhibitor - M2 = No; CYP2C19 inhibitor - M2 = No; CYP2C9 inhibitor - M2 = Yes; CYP2D6 inhibitor - M2 = No; CYP3A4 inhibitor - M2 = No; log Kp (cm/s) for M2 = -2.29; Lipinski's Rule violations by M2 = 1; Ghose's Rule violations by M2 = 1; Veber's Rule violations by M2 = 1; Egan's Rule violations by M2 = 1; Muegge's Rule violations by M2 = 2; PAINS # alerts for M2 = 0; Brenk # alerts for M2 = 1; Leadlikeness violations by M2 = 2; SA Score in M2 = 4.3; Bioavailability Score in M2 = 0.55 (Fig.1b; Table 2-6).

ADMET informatics of 3,7,11,15-Tetramethyl-2-hexadecen-1-ol (M3)

MW of M3 = 296.53; # Heavy atoms in M3 = 21; # aromatic Heavy atoms in M3 = 0; Fraction Csp3 in M3 = 0.9; # rotatable bonds in M3 = 13; # H-bond acceptors in M3 = 1; # H-bond donors in M3 = 1; Molar refractivity in M3 = 98.94; Topological polar surface area of M3 = 20.23; Log Po/w value for M3 = 4.66; The octanol–water partition coefficient (XLOGP3) for M3 = 8.19; lipophilicity of large molecules (WLOGP) for M3 = 6.36; Moriguchi octanol-water partition coefficient (MLOGP) for M3 = 5.25; Silicos-IT Log P in M3 = 6.57; Consensus Log P in M3 = 6.21; ESOL Log S in M3 = -5.98; ESOL Solubility (mg/ml) for M3 = 3.10E-04; ESOL Solubility (mol/l) for M3 = 1.05E-06; ESOL Class value for M3 = MS; Ali Log S in M3 = -8.47; Ali Solubility (mg/ml) for M3 = 9.94E-07; Ali Solubility (mol/l) for M3 = 3.35E-09; Ali Class value for M3 = PS; Silicos-IT LogSw in M3 = -5.51; Silicos-IT Solubility (mg/ml) for M3 = 9.06E-04; Silicos-IT Solubility (mol/l) for M3 = 3.05E-06; Silicos-IT class value for M3 = MS; GI absorption by M3 = Low; BBB permeant in M3 = No; Pgp substrate in M3 = Yes; CYP1A2 inhibitor - M3 = No; CYP2C19 inhibitor - M3 = No; CYP2C9 inhibitor - M3 = Yes; CYP2D6 inhibitor - M3 = No; CYP3A4 inhibitor - M3 = No; log Kp (cm/s) for M3 = -2.29; Lipinski's Rule violations by M3 = 1; Ghose's Rule violations by M3 = 1; Veber's Rule violations by M3 = 1; Egan's Rule violations by M3 = 1; Muegge's Rule violations by M3 = 2; PAINS # alerts for M3 = 0; Brenk # alerts for M3 = 1; Leadlikeness violations by M3 = 2; SA Score in M3 = 4.3; Bioavailability Score in M3 = 0.55 (Fig.1c; Table 2-6).

ADMET informatics of 6,9,12,15-Docosatetraenoic acid, me (M4)

MW of M4 = 332.52; # Heavy atoms in M4 = 24; # aromatic Heavy atoms in M4 = 0; Fraction Csp3 in M4 = 0.59; # rotatable bonds in M4 = 16; # H-bond acceptors in M4 = 2; # H-bond donors in M4 = 1; Molar refractivity in M4 = 107.74; Topological polar surface area of M4 = 37.3; Log Po/w value for M4 = 4.99; The octanol–water partition coefficient (XLOGP3) for M4 = 7.94; lipophilicity of large molecules (WLOGP) for M4 = 7; Moriguchi octanol-water partition coefficient (MLOGP) for M4 = 5.2; Silicos-IT Log P in M4 = 7.17; Consensus Log P in M4 = 6.46; ESOL Log S in M4 = -5.85; ESOL Solubility (mg/ml) for M4 = 4.72E-04; ESOL Solubility (mol/l) for M4 = 1.42E-06; ESOL Class value for M4 = MS; Ali Log S in M4 = -8.57; Ali Solubility (mg/ml) for M4 = 8.87E-07; Ali Solubility (mol/l) for M4 = 2.67E-09; Ali Class value for M4 = PS; Silicos-IT LogSw in M4 = -4.83; Silicos-IT Solubility (mg/ml) for M4 = 4.92E-03; Silicos-IT Solubility (mol/l) for M4 = 1.48E-05; Silicos-IT class value for M4 = MS; GI absorption by M4 = Low; BBB permeant in M4 = No; Pgp substrate in M4 = No; CYP1A2 inhibitor - M4 = Yes; CYP2C19 inhibitor - M4 = No; CYP2C9 inhibitor - M4 = Yes; CYP2D6 inhibitor - M4 = No; CYP3A4 inhibitor - M4 = No; log Kp (cm/s) for M4 = -2.69; Lipinski's Rule violations by M4 = 1; Ghose's Rule violations by M4 = 1; Veber's Rule violations by M4 = 1; Egan's Rule violations by M4 = 1; Muegge's Rule violations by M4 = 2; PAINS # alerts for M4 = 0; Brenk # alerts for M4 = 1; Leadlikeness violations by M4 = 2; SA Score in M4 = 3.41; Bioavailability Score in M4 = 0.85 (Fig.1d; Table 2-6).

ADMET informatics of Cyclohexanol, 5-methyl-2-(1-methylethyl)- (M5)

MW of M5 = 198.3; # Heavy atoms in M5 = 14; # aromatic Heavy atoms in M5 = 0; Fraction Csp3 in M5 = 0.92; # rotatable bonds in M5 = 3; # H-bond acceptors in M5 = 2; # H-bond donors in M5 = 0; Molar refractivity in M5 = 58.97; Topological polar surface area of M5 = 26.3; Log Po/w value for M5 = 2.68; The octanol–water partition coefficient (XLOGP3) for M5 = 4; lipophilicity of large molecules (WLOGP) for M5 = 3.01; Moriguchi octanol-water partition coefficient (MLOGP) for M5 = 2.76; Silicos-IT Log P in M5 = 2.49; Consensus Log P in M5 = 2.99; ESOL Log S in M5 = -3.39; ESOL Solubility (mg/ml) for M5 = 8.05E-02; ESOL Solubility (mol/l) for M5 = 4.06E-04; ESOL Class value for M5 = S; Ali Log S in M5 = -4.25; Ali Solubility (mg/ml) for M5 = 1.10E-02; Ali Solubility (mol/l) for M5 = 5.57E-05; Ali Class value for M5 = MS; Silicos-IT LogSw in M5 = -2.15; Silicos-IT Solubility (mg/ml) for M5 = 1.41E+00; Silicos-IT Solubility (mol/l) for M5 = 7.13E-03; Silicos-IT class value for M5 = S; GI absorption by M5 = High; BBB permeant in M5 = Yes; Pgp substrate in M5 = No; CYP1A2 inhibitor - M5 = No; CYP2C19 inhibitor - M5 = No; CYP2C9 inhibitor - M5 = Yes; CYP2D6 inhibitor - M5 = No; CYP3A4 inhibitor - M5 = No; log Kp (cm/s) for M5 = -4.67; Lipinski's Rule violations by M5 = 0; Ghose's Rule violations by M5 = 0; Veber's Rule violations by M5 = 0; Egan's Rule violations by M5 = 0; Muegge's Rule violations by M5 = 1; PAINS # alerts for M5 = 0; Brenk # alerts for M5 = 0; Leadlikeness violations by M5 = 2; SA Score in M5 = 2.92; Bioavailability Score in M5 = 0.55 (Fig.1e; Table 2-6).

ADMET informatics of 3,7,11,15-Tetramethyl-2-hexadecen-1-ol (M6)

MW of M6 = 296.53; # Heavy atoms in M6 = 21; # aromatic Heavy atoms in M6 = 0; Fraction Csp3 in M6 = 0.9; # rotatable bonds in M6 = 13; # H-bond acceptors in M6 = 1; # H-bond donors in M6 = 1; Molar refractivity in M6 = 98.94; Topological polar surface area of M6 = 20.23; Log Po/w value for M6 = 4.66; The octanol–water partition coefficient (XLOGP3) for M6 = 8.19; lipophilicity of large molecules (WLOGP) for M6 = 6.36; Moriguchi octanol-water partition coefficient (MLOGP) for M6 = 5.25; Silicos-IT Log P in M6 = 6.57; Consensus Log P in M6 = 6.21; ESOL Log S in M6 = -5.98; ESOL Solubility (mg/ml) for M6 = 3.10E-04; ESOL Solubility (mol/l) for M6 = 1.05E-06; ESOL Class value for M6 = MS; Ali Log S in M6 = -8.47; Ali Solubility (mg/ml) for M6 = 9.94E-07; Ali Solubility (mol/l) for M6 = 3.35E-09; Ali Class value for M6 = PS; Silicos-IT LogSw in M6 = -5.51; Silicos-IT Solubility (mg/ml) for M6 = 9.06E-04; Silicos-IT Solubility (mol/l) for M6 = 3.05E-06; Silicos-IT class value for M6 = MS; GI absorption by M6 = Low; BBB permeant in M6 = No; Pgp substrate in M6 = Yes; CYP1A2 inhibitor - M6 = No; CYP2C19 inhibitor - M6 = No; CYP2C9 inhibitor - M6 = Yes; CYP2D6 inhibitor - M6 = No; CYP3A4 inhibitor - M6 = No; log Kp (cm/s) for M6 = -2.29; Lipinski's Rule violations by M6 = 1; Ghose's Rule violations by M6 = 1; Veber's Rule violations by M6 = 1; Egan's Rule violations by M6 = 1; Muegge's Rule violations by M6 = 2; PAINS # alerts for M6 = 0; Brenk # alerts for M6 = 1; Leadlikeness violations by M6 = 2; SA Score in M6 = 4.3; Bioavailability Score in M6 = 0.55 (Fig.1f; Table 2-6).

ADMET informatics of Palmitic acid vinyl ester (M7)

MW of M7 = 282.46; # Heavy atoms in M7 = 20; # aromatic Heavy atoms in M7 = 0; Fraction Csp3 in M7 = 0.83; # rotatable bonds in M7 = 16; # H-bond acceptors in M7 = 2; # H-bond donors in M7 = 0; Molar refractivity in M7 = 89.45; Topological polar surface area of M7 = 26.3; Log Po/w value for M7 = 4.8; The octanol–water partition coefficient (XLOGP3) for M7 = 7.87; lipophilicity of large molecules (WLOGP) for M7 = 6.15; Moriguchi octanol-water partition coefficient (MLOGP) for M7 = 4.57; Silicos-IT Log P in M7 = 6.27; Consensus Log P in M7 = 5.93; ESOL Log S in M7 = -5.49; ESOL Solubility (mg/ml) for M7 = 9.07E-04; ESOL Solubility (mol/l) for M7 = 3.21E-06; ESOL Class value for M7 = MS; Ali Log S in M7 = -8.27; Ali Solubility (mg/ml) for M7 = 1.52E-06; Ali Solubility (mol/l) for M7 = 5.37E-09; Ali Class value for M7 = PS; Silicos-IT LogSw in M7 = -6.07; Silicos-IT Solubility (mg/ml) for M7 = 2.43E-04; Silicos-IT Solubility (mol/l) for M7 = 8.59E-07; Silicos-IT class value for M7 = PS; GI absorption by M7 = High; BBB permeant in M7 = No; Pgp substrate in M7 = No; CYP1A2 inhibitor - M7 = Yes; CYP2C19 inhibitor - M7 = No; CYP2C9 inhibitor - M7 = Yes; CYP2D6 inhibitor - M7 = No; CYP3A4 inhibitor - M7 = No; log Kp (cm/s) for M7 = -2.44; Lipinski's Rule violations by M7 = 1; Ghose's Rule violations by M7 = 1; Veber's Rule violations by M7 = 1; Egan's Rule violations by M7 = 1; Muegge's Rule violations by M7 = 2; PAINS # alerts for M7 = 0; Brenk # alerts for M7 = 1; Leadlikeness violations by M7 = 2; SA Score in M7 = 3.44; Bioavailability Score in M7 = 0.55 (Fig.1g; Table 2-6).

ADMET informatics of γ Tocopherol (M8)

MW of M8 = 416.68; # Heavy atoms in M8 = 30; # aromatic Heavy atoms in M8 = 6; Fraction Csp3 in M8 = 0.79; # rotatable bonds in M8 = 12; # H-bond acceptors in M8 = 2; # H-bond donors in M8 = 1; Molar refractivity in M8 = 134.31; Topological polar surface area of M8 = 29.46; Log Po/w value for M8 = 5.76; The octanol–water partition coefficient (XLOGP3) for M8 = 10.33; lipophilicity of large molecules (WLOGP) for M8 = 8.53; Moriguchi octanol-water partition coefficient (MLOGP) for M8 = 5.94; Silicos-IT Log P in M8 = 9.2; Consensus Log P in M8 = 7.95; ESOL Log S in M8 = -8.29; ESOL Solubility (mg/ml) for M8 = 2.15E-06; ESOL Solubility (mol/l) for M8 = 5.16E-09; ESOL Class value for M8 = PS; Ali Log S in M8 = -10.89; Ali Solubility (mg/ml) for M8 = 5.38E-09; Ali Solubility (mol/l) for M8 = 1.29E-11; Ali Class value for M8 = IS; Silicos-IT LogSw in M8 = -8.79; Silicos-IT Solubility (mg/ml) for M8 = 6.80E-07; Silicos-IT Solubility (mol/l) for M8 = 1.63E-09; Silicos-IT class value for M8 = PS; GI absorption by M8 = Low; BBB permeant in M8 = No; Pgp substrate in M8 = Yes; CYP1A2 inhibitor - M8 = No; CYP2C19 inhibitor - M8 = No; CYP2C9 inhibitor - M8 = No; CYP2D6 inhibitor - M8 = No; CYP3A4 inhibitor - M8 = No; log Kp (cm/s) for M8 = -1.51; Lipinski's Rule violations by M8 = 1; Ghose's Rule violations by M8 = 3; Veber's Rule violations by M8 = 1; Egan's Rule violations by M8 = 1; Muegge's Rule violations by M8 = 1; PAINS # alerts for M8 = 0; Brenk # alerts for M8 = 0; Leadlikeness violations by M8 = 3; SA Score in M8 = 5; Bioavailability Score in M8 = 0.55 (Fig.1h; Table 2-6).

ADMET informatics of ADMET informatics of Vitamin E (M9)

MW of M9 = 430.71; # Heavy atoms in M9 = 31; # aromatic Heavy atoms in M9 = 6; Fraction Csp3 in M9 = 0.79; # rotatable bonds in M9 = 12; # H-bond acceptors in M9 = 2; # H-bond donors in M9 = 1; Molar refractivity in M9 = 139.27; Topological polar surface area of M9 = 29.46; Log Po/w value for M9 = 6.04; The octanol–water partition coefficient (XLOGP3) for M9 = 10.7; lipophilicity of large molecules (WLOGP) for M9 = 8.84; Moriguchi octanol-water partition coefficient (MLOGP) for M9 = 6.14; Silicos-IT Log P in M9 = 9.75; Consensus Log P in M9 = 8.29; ESOL Log S in M9 = -8.6; ESOL Solubility (mg/ml) for M9 = 1.08E-06; ESOL Solubility (mol/l) for M9 = 2.50E-09; ESOL Class value for M9 = PS; Ali Log S in M9 = -11.27; Ali Solubility (mg/ml) for M9 = 2.30E-09; Ali Solubility (mol/l) for M9 = 5.33E-12; Ali Class value for M9 = IS; Silicos-IT LogSw in M9 = -9.16; Silicos-IT Solubility (mg/ml) for M9 = 2.97E-07; Silicos-IT Solubility (mol/l) for

M9 = 6.89E-10; Silicos-IT class value for M9 = PS; GI absorption by M9 = Low; BBB permeant in M9 = No; Pgp substrate in M9 = Yes; CYP1A2 inhibitor - M9 = No; CYP2C19 inhibitor - M9 = No; CYP2C9 inhibitor - M9 = No; CYP2D6 inhibitor - M9 = No; CYP3A4 inhibitor - M9 = No; log Kp (cm/s) for M9 = -1.33; Lipinski's Rule violations by M9 = 1; Ghose's Rule violations by M9 = 3; Veber's Rule violations by M9 = 1; Egan's Rule violations by M9 = 1; Muegge's Rule violations by M9 = 1; PAINS # alerts for M9 = 0; Brenk # alerts for M9 = 0; Leadlikeness violations by M9 = 3; SA Score in M9 = 5.17; Bioavailability Score in M9 = 0.55 (Fig.1i; Table 2-6).

ADMET informatics of Cholesta-7,9(11)-dien-3-ol, 4,4-dim (M10)

MW of M10 = 412.69; # Heavy atoms in M10 = 30; # aromatic Heavy atoms in M10 = 0; Fraction Csp3 in M10 = 0.86; # rotatable bonds in M10 = 5; # H-bond acceptors in M10 = 1; # H-bond donors in M10 = 1; Molar refractivity in M10 = 132.49; Topological polar surface area of M10 = 20.23; Log Po/w value for M10 = 5.07; The octanol–water partition coefficient (XLOGP3) for M10 = 8.53; lipophilicity of large molecules (WLOGP) for M10 = 7.94; Moriguchi octanol-water partition coefficient (MLOGP) for M10 = 6.62; Silicos-IT Log P in M10 = 7.03; Consensus Log P in M10 = 7.04; ESOL Log S in M10 = -7.44; ESOL Solubility (mg/ml) for M10 = 1.49E-05; ESOL Solubility (mol/l) for M10 = 3.61E-08; ESOL Class value for M10 = PS; Ali Log S in M10 = -8.83; Ali Solubility (mg/ml) for M10 = 6.14E-07; Ali Solubility (mol/l) for M10 = 1.49E-09; Ali Class value for M10 = PS; Silicos-IT LogSw in M10 = -6.5; Silicos-IT Solubility (mg/ml) for M10 = 1.31E-04; Silicos-IT Solubility (mol/l) for M10 = 3.18E-07; Silicos-IT class value for M10 = PS; GI absorption by M10 = Low; BBB permeant in M10 = No; Pgp substrate in M10 = No; CYP1A2 inhibitor - M10 = No; CYP2C19 inhibitor - M10 = No; CYP2C9 inhibitor - M10 = No; CYP2D6 inhibitor - M10 = No; CYP3A4 inhibitor - M10 = No; log Kp (cm/s) for M10 = -2.76; Lipinski's Rule violations by M10 = 1; Ghose's Rule violations by M10 = 3; Veber's Rule violations by M10 = 0; Egan's Rule violations by M10 = 1; Muegge's Rule violations by M10 = 2; PAINS # alerts for M10 = 0; Brenk # alerts for M10 = 0; Leadlikeness violations by M10 = 2; SA Score in M10 = 6.32; Bioavailability Score in M10 = 0.55 (Fig.1j; Table 2-6).

ADMET informatics of γ-Sitosterol (M11)

MW of M11 = 432.72; # Heavy atoms in M11 = 31; # aromatic Heavy atoms in M11 = 0; Fraction Csp3 in M11 = 0.93; # rotatable bonds in M11 = 6; # H-bond acceptors in M11 = 2; # H-bond donors in M11 = 2; Molar refractivity in M11 = 136.28; Topological polar surface area of M11 = 29.46; Log Po/w value for M11 = 5.03; The octanol–water partition coefficient (XLOGP3) for M11 = 8.86; lipophilicity of large molecules (WLOGP) for M11 = 7.96; Moriguchi octanol-water partition coefficient (MLOGP) for M11 = 5.8; Silicos-IT Log P in M11 = 7.04; Consensus Log P in M11 = 6.94; ESOL Log S in M11 = -7.71; ESOL Solubility (mg/ml) for M11 = 8.46E-06; ESOL Solubility (mol/l) for M11 = 1.96E-08; ESOL Class value for M11 = PS; Ali Log S in M11 = -9.36; Ali Solubility (mg/ml) for M11 = 1.87E-07; Ali Solubility (mol/l) for M11 = 4.33E-10; Ali Class value for M11 = PS; Silicos-IT LogSw in M11 = -6.19; Silicos-IT Solubility (mg/ml) for M11 = 2.81E-04; Silicos-IT Solubility (mol/l) for M11 = 6.49E-07; Silicos-IT class value for M11 = PS; GI absorption by M11 = Low; BBB permeant in M11 = No; Pgp substrate in M11 = No; CYP1A2 inhibitor - M11 = No; CYP2C19 inhibitor - M11 = No; CYP2C9 inhibitor - M11 = No; CYP2D6 inhibitor - M11 = No; CYP3A4 inhibitor - M11 = No; log Kp (cm/s) for M11 = -2.65; Lipinski's Rule violations by M11 = 1; Ghose's Rule violations by M11 = 3; Veber's Rule violations by M11 = 0; Egan's Rule violations by M11 = 1; Muegge's Rule violations by M11 = 1; PAINS # alerts for M11 = 0; Brenk # alerts for M11 = 1; Leadlikeness violations by M11 = 2; SA Score in M11 = 6.42; Bioavailability Score in M11 = 0.55 (Fig.1k; Table 2-6).

ADMET informatics of Stigmasta-5,24(28)-dien-3-ol, (3.β-24Z)- (M12)

MW of M12 = 412.69; # Heavy atoms in M12 = 30; # aromatic Heavy atoms in M12 = 0; Fraction Csp3 in M12 = 0.86; # rotatable bonds in M12 = 5; # H-bond acceptors in M12 = 1; # H-bond donors in M12 = 1; Molar refractivity in M12 = 132.75; Topological polar surface area of M12 = 20.23; Log Po/w value for M12 = 5.08; The octanol–water partition coefficient (XLOGP3) for M12 = 8.85; lipophilicity of large molecules (WLOGP) for M12 = 7.94; Moriguchi octanol-water partition coefficient (MLOGP) for M12 = 6.62; Silicos-IT Log P in M12 = 6.88; Consensus Log P in M12 = 7.08; ESOL Log S in M12 = -7.64; ESOL Solubility (mg/ml) for M12 = 9.36E-06; ESOL Solubility (mol/l) for M12 = 2.27E-08; ESOL Class value for M12 = PS; Ali Log S in M12 = -9.16; Ali Solubility (mg/ml) for M12 = 2.86E-07; Ali Solubility (mol/l) for M12 = 6.92E-10; Ali Class value for M12 = PS; Silicos-IT LogSw in M12 = -5.83; Silicos-IT Solubility (mg/ml) for M12 = 6.16E-04; Silicos-IT Solubility (mol/l) for M12 = 1.49E-06; Silicos-IT class value for M12 = MS; GI absorption by M12 = Low; BBB permeant in M12 = No; Pgp substrate in M12 = No; CYP1A2 inhibitor - M12 = No; CYP2C19 inhibitor - M12 = No; CYP2C9 inhibitor - M12 = No; CYP2D6 inhibitor - M12 = No; CYP3A4 inhibitor - M12 = No; log Kp (cm/s) for M12 = -2.53; Lipinski's Rule violations by M12 = 1; Ghose's Rule violations by M12 = 3; Veber's Rule violations by M12 = 0; Egan's Rule violations by M12 = 1; Muegge's Rule violations by M12 = 2; PAINS # alerts for M12 = 0; Brenk # alerts for M12 = 1; Leadlikeness violations by M12 = 2; SA Score in M12 = 6.15; Bioavailability Score in M12 = 0.55 (Fig.1l; Table 2-6). BIOLED-Egg illustration of all the bioactive compounds in MONDRP is given in Fig. 2. Natural Product likeness density chart of bioactive compounds in MONDRP is given in Fig. 3 and the Swiss Target Prediction and Distribution Chart of all the selected bioactive compounds in MONDRP is given in Fig. a-l.

Mutagenicity refers to the induction of permanent transmissible changes in the structure of the genetic material; Tumorigenicity refers to the process by which neoplastic cells are grown from tumors; Irritant refers to a stimulus from compound that causes irritation; Reproductive effective refers to adverse effect of compounds that interfere with the reproduction in an organism; logS value is estimated, and it is a unit-stripped logarithm (base 10) of the solubility measured in mol/liter. It is a value of the compound's drug-like properties. The drug likeness is calculated by summing up score values of bioactive molecules in the present investigation. Drug score is composed of drug likeness, cLogP, logS, molecular weight and factors of toxicity risk management, and is used to judge the compound's overall potential to qualify for a drug candidate. The value of the drug score is between 0 and 1, and the larger value means better pharmacokinetic properties (Table 7).

CONCLUSION

Summative ADMET properties of all bioactive compounds *Moringa oleifera* Natural-Ripened-Dried (MONRD**)** Methanolic Pod Extract (MOMPE) as a potential source of natural drug lead namely - 7-Octadecyne, 2-methyl- ($C_{19}H_{36}$); 3,7,11,15-Tetramethyl-2-hexadecen-1-ol ($C_{20}H_{40}O$); 3,7,11,15-Tetramethyl-2-hexadecen-1-ol ($C_{20}H_{40}O$); 6,9,12,15-Docosatetraenoic acid, me ($C_{23}H_{38}O_2$); Cyclohexanol, 5-methyl-2-(1-methylethyl)- ($C_{10}H_{20}O$); 3,7,11,15-Tetramethyl-2-

hexadecen-1-ol ($C_{20}H_{40}O$); Palmitic acid vinyl ester ($C_{18}H_{34}O_2$); .γ.-Tocopherol ($C_{28}H_{48}O_2$); Vitamin E ($C_{29}H_{50}O_2$); Cholesta-7,9(11)-dien-3-ol, 4,4-dim ($C_{29}H_{48}O$); γ.-Sitosterol ($C_{29}H_{50}O$); Stigmasta-5,24(28)-dien-3-ol, (3.β.,24Z)- ($C_{29}H_{48}O$) has been provided. All the compounds exhibited good gastrointestinal absorption with enhanced pharmacokinetic properties and low blood-brain barrier permeability. Further, work on the biomolecular and bioactivity aspects of these compounds in MONRD pod is expected to provide holistic baseline information for successful exploitation of lead candidates in drug design, development program.

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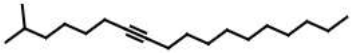
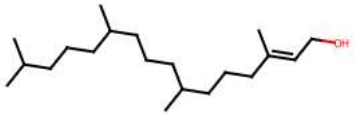
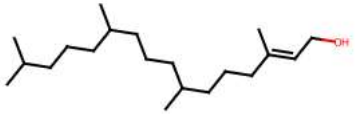
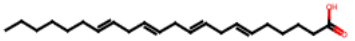
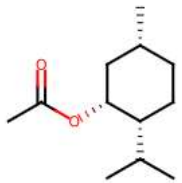
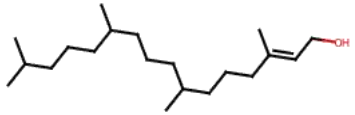
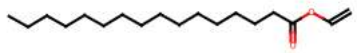
Table 1 List of Bioactive Compounds in *Moringa oleifera* Natural-Ripened-Dried Methanolic Pod Extract (MOMPE) with 2D structure

Name of the Compound	Code for the Compound	SMILES	2D Structure
7-Octadecyne, 2-methyl-	**MOMPE** 1	CCCCCCCCCCC#CCCCCC(C)C	
3,7,11,15-Tetramethyl-2-hexadecen-1-ol	**MOMPE** 2	C/C(=C\CO)CCCC(C)CCCC(C)CCCC(C)C	
3,7,11,15-Tetramethyl-2-hexadecen-1-ol	**MOMPE** 3	C/C(=C\CO)CCCC(C)CCCC(C)CCCC(C)C	
6,9,12,15-Docosatetraenoic acid, me	**MOMPE** 4	CCCCCCC=CCC=CCC=CCC=CCCCCC(=O)O	
Cyclohexanol, 5-methyl-2-(1-methylethyl)-	**MOMPE** 5	CC(=O)O[C@@H]1C[C@H](C)CC[C@@H]1C(C)C	
3,7,11,15-Tetramethyl-2-hexadecen-1-ol	**MOMPE** 6	C/C(=C\CO)CCCC(C)CCCC(C)CCCC(C)C	
Palmitic acid vinyl ester	**MOMPE** 7	C=COC(=O)CCCCCCCCCCCCCCC	

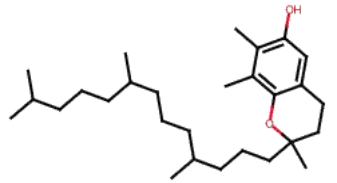
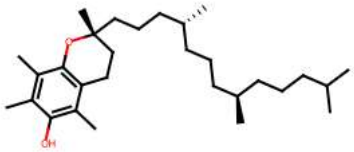
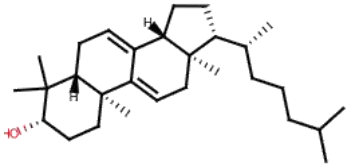
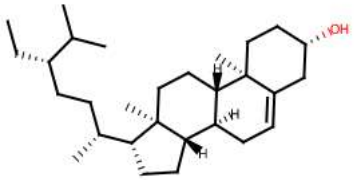
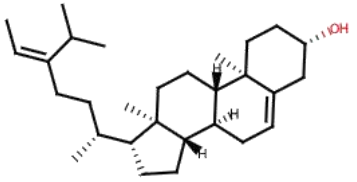
γ Tocopherol	**MOMPE** 8	Cc1c(O)cc2c(c1C)OC(C)(CCCC(C)CCCC(C)CCCC(C)C)CC2	
Vitamin E	**MOMPE** 9	Cc1c(C)c2c(c(C)c1O)CC[C@@](C)(CCC[C@H](C)CCC[C@H](C)CCCC(C)C)O2	
Cholesta-7,9(11)-dien-3-ol, 4,4-dim	**MOMPE** 10	CC(C)CCC[C@@H](C)[C@H]1CC[C@H]2C3=CC[C@H]4C(C)(C)[C@@H](O)CC[C@]4(C)C3=CC[C@@]21C	
γ-Sitosterol	**MOMPE** 11	CC[C@@H](CC[C@@H](C)[C@H]1CC[C@H]2[C@@H]3CC=C4C[C@@H](O)CC[C@]4(C)[C@H]3CC[C@@]21C)C(C)C	
Stigmasta-5,24(28)-dien-3-ol, (3.β-24Z)-	**MOMPE** 12	C/C=C(/CC[C@@H](C)[C@H]1CC[C@H]2[C@@H]3CC=C4C[C@@H](O)CC[C@]4(C)[C@H]3CC[C@@]21C)C(C)C	

Table 2 Predicted Pharmacokinetic Properties for Absorption of bioactive compounds in MOMPE

Code of the Compound	Water solubility	Caco2 permeability (human)	Intestinal absorption (human)	Skin Permeability (human)	P-glycoprotein		
					substrate	Inhibitor I	Inhibitor II
MOMPE 1	-8.343	1.402	92.262	-2.599	No	No	No
MOMPE 2	-7.554	1.515	90.71	-2.576	No	No	Yes
MOMPE 3	-7.554	1.515	90.71	-2.576	No	No	Yes
MOMPE 4	-6.175	1.121	91.967	-2.732	No	No	No
MOMPE 5	-2.818	1.698	96.497	-2.208	No	No	No
MOMPE 6	-7.554	1.515	90.71	-2.576	No	No	Yes
MOMPE 7	-7.183	1.596	91.599	-2.682	No	No	No
MOMPE 8	-7.602	1.458	90.043	-2.62	No	Yes	Yes
MOMPE 9	-6.901	1.345	89.782	-2.683	No	No	Yes
MOMPE 10	-7.208	1.205	93.542	-2.881	No	Yes	Yes
MOMPE 11	-6.461	1.18	95.718	-2.826	No	Yes	Yes
MOMPE 12	-6.715	1.212	94.642	-2.781	No	Yes	Yes

Table 3 Predicted Pharmacokinetic Properties for Distribution of bioactive compounds in MOMPE

Code of the Compound	VDss (human)	Fraction unbound (human)	BBB permeability (human)	CNS permeability (human)	
MOMPE 1	0.491	0	0.968	-0.887	
MOMPE 2	0.468	0	0.806	-1.563	
MOMPE 3	0.468	0	0.806	-1.563	
MOMPE 4	-0.659	0.002	-0.256	-1.276	
MOMPE 5	0.125	0.439	0.539	-2.39	
MOMPE 6	0.468	0	0.806	-1.563	
MOMPE 7	0.376	0.054	0.752	-1.777	
MOMPE 8	0.732	0	0.739	-1.669	
MOMPE 9	0.709	0	0.876	-1.669	
MOMPE 10	0.489	0	0.738	-1.961	
MOMPE 11	0.069	0	-0.462	-1.497	
MOMPE 12					

Table 4 Predicted Pharmacokinetic Properties for Metabolism and Excretion of bioactive compounds in MOMPE

Code of the Compound	CYP2D6 substrate	CYP3A4 substrate	CYP1A2 inhibitior	CYP2C19 inhibitior	CYP2C9 inhibitior	CYP2D6 inhibitior	CYP3A4 inhibitior	Total Clearance	Renal OCT2 substrate
MOMPE 1	No	Yes	Yes	No	No	No	No	1.789	No
MOMPE 2	No	Yes	Yes	No	No	No	No	1.686	No
MOMPE 3	No	Yes	Yes	No	No	No	No	1.686	No
MOMPE 4	No	Yes	Yes	No	No	No	No	2.165	No
MOMPE 5	No	No	No	No	No	No	No	1.207	No
MOMPE 6	No	Yes	Yes	No	No	No	No	1.686	No
MOMPE 7	No	Yes	Yes	No	No	No	No	1.947	No
MOMPE 8	No	Yes	No	No	No	No	No	0.821	No
MOMPE 9	No	Yes	No	Yes	No	No	No	0.794	No
MOMPE 10	No	Yes	No	No	No	No	No	0.422	No
MOMPE 11	No	Yes	No	No	No	No	No	0.662	No
MOMPE 12	No	Yes	No	No	No	No	No	0.619	No

Table 5 Predicted Pharmacokinetic Properties for Toxicity of bioactive compounds in MOMPE

Code of the Compound	AMES toxicity	Max. tolerated dose (human)	hERG I inhibitor	hERG II inhibitor	Oral Rat Acute Toxicity (LD_{50})	Oral Rat Chronic Toxicity (LOAEL)	Hepatotoxicity	Skin Sensitisation	*T.pyriformis* toxicity	Minnow toxicity
MOMPE 1	No	-0.286	No	Yes	1.504	1.294	No	Yes	1.235	-1.75
MOMPE 2	No	0.05	No	Yes	1.607	1.043	No	Yes	1.884	-1.504
MOMPE 3	No	0.05	No	Yes	1.607	1.043	No	Yes	1.884	-1.504
MOMPE 4	No	-0.928	No	No	1.427	3.352	No	Yes	0.429	-2.019
MOMPE 5	No	0.747	No	No	1.823	2.04	No	Yes	0.877	1.335
MOMPE 6	No	0.05	No	Yes	1.607	1.043	No	Yes	1.884	-1.504
MOMPE 7	No	0.205	No	No	1.689	3.051	No	Yes	1.83	-1.546
MOMPE 8	No	0.781	No	Yes	2.21	2.052	No	No	0.946	-3.814
MOMPE 9	No	0.775	No	Yes	2.072	1.987	No	No	1.017	-3.324
MOMPE 10	No	-0.586	No	Yes	2.01	0.851	No	No	0.651	-1.731
MOMPE 11	No	-0.81	No	Yes	2.658	0.637	No	No	0.428	-1.585
MOMPE 12	No	-0.653	No	Yes	2.553	0.89	No	No	0.432	-1.711

Table 6 Predicted Medicinal Chemistry of bioactive compounds in MOMPE

PROPERTY	MOMPE 1	MOMPE 2	MOMPE 3	MOMPE 4	MOMPE 5	MOMPE 6	MOMPE 7	MOMPE 8	MOMPE 9	MOMPE 10	MOMPE 11	MOMPE 12
QED	0.27	0.392	0.392	0.244	0.637	0.392	0.204	0.37	0.359	0.486	0.436	0.454
SA Score	2.232	3.291	3.291	2.739	3.141	3.291	2.149	3.786	3.78	4.563	4.388	4.494
Fsp^3	0.895	0.9	0.9	0.591	0.917	0.9	0.833	0.786	0.793	0.862	0.931	0.862
MCE-18	0	4	4	0	20.174	4	0	53.04	56.077	71.963	68.464	69
NP Score	0.678	1.532	1.532	0.989	1.542	1.532	0.606	1.571	1.5	3.012	2.681	2.897
Lipinski Rule	0	0	0	0	0	0	0	1	1	0	0	0
Pfizer Rule	1	1	1	0	0	1	1	1	1	0	0	0
GSK Rule	0	0	0	0	0	0	0	0	0	0	0	0
Golden Triangle	0	0	0	0	0	0	0	0	0	0	0	0
PAINS	Accepted	Accepted	Accepted	Accepted	Accepted	Accepted	Accepted	Accepted	Accepted	Accepted	Accepted	Accepted
ANMR Rule	Rejected	Rejected	Rejected	Rejected	Rejected	Rejected	Rejected	Rejected	Rejected	Rejected	Rejected	Rejected
BMS Rule	Rejected	Rejected	Rejected	Rejected	Accepted	Rejected	Rejected	Rejected	Rejected	Rejected	Rejected	Rejected
Chelator Rule	Rejected	Rejected	Rejected	Accepted	Rejected	Rejected	Accepted	Rejected	Rejected	Rejected	Rejected	Rejected

Table 7 Summative contribution of different parameters to drug score of bioactive compounds in MOMPE

Prediction Property	MOMPE 1	MOMPE 2	MOMPE 3	MOMPE 4	MOMPE 5	MOMPE 6	MOMPE 7	MOMPE 8	MOMPE 9	MOMPE 10	MOMPE 11	MOMPE 12
cLogP	8.098	7.421	7.421	7.78	2.895	7.421	6.717	9.299	9.643	7.678	7.855	7.991
S cLogP	0.043	0.081	0.081	0.058	0.891	0.081	0.152	0.013	0.009	0.064	0.054	0.047
LogS	-7.11	-4.633	-4.633	-4.946	-2.91	-4.633	-5.057	-6.852	-7.169	-6.312	-6.669	--6.405
S LogS	0.108	0.59	0.59	0.513	0.889	0.59	0.485	0.135	0.100	0.212	0.158	0.197
Mol Wt	264.0	296.0	296.0	332.0	198.0	296.0	282.0	416.0	430.0	412.0	414.0	412.0
S Mol Wt	0.944	0.92	0.92	0.882	0.974	0.92	0.931	0.732	0.698	0.741	0.737	0.741
Drug-Like	-25.95	-3.766	-3.766	-24.86	-21.92	-3.766	-28.151	-3.275	-4.783	-3.02	-4.475	-6.284
S Drug-Like	0.0	0.022	0.022	0.0	0.0	0.022	0.0	0.036	0.008	0.046	0.011	0.001
NRM	1.0	1.0	1.0	1.0	1.0	1.0	0.6	1.0	1.0	1.0	1.0	1.0
NRT	1.0	1.0	1.0	1.0	1.0	1.0	0.6	1.0	1.0	1.0	1.0	1.0
NRIE	1.0	1.0	1.0	1.0	0.8	1.0	0.8	1.0	1.0	1.0	1.0	0.6
NRRE	1.0	1.0	1.0	1.0	1.0	1.0	0.8	1.0	1.0	1.0	1.0	1.0
Drug Score	0.14	0.211	0.211	0.188	0.352	0.211	0.047	0.129	0.118	0.146	0.134	0.082

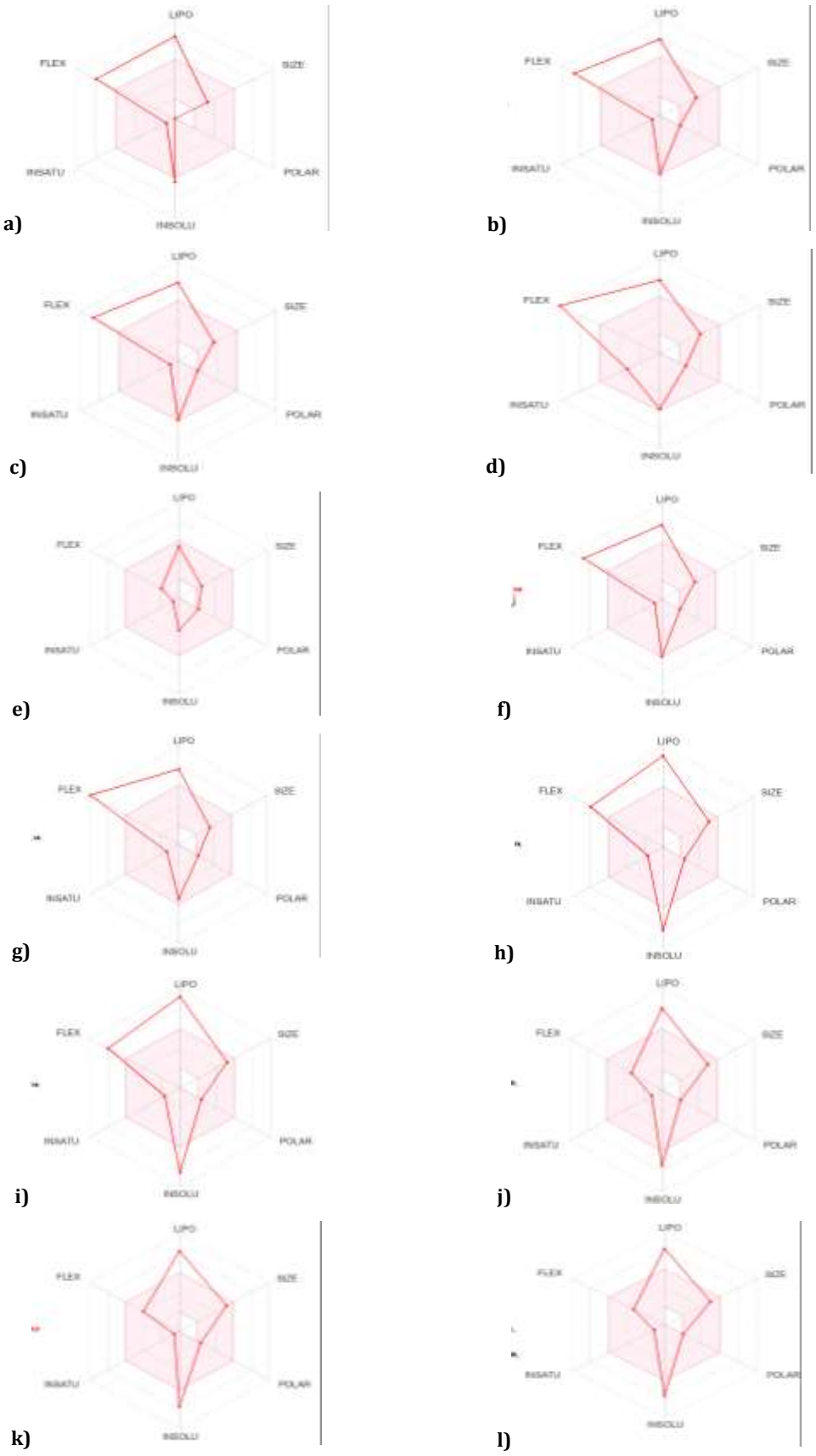


Figure 1(a-l): Bioavailability radar chart of bioactive compounds in MONDRP

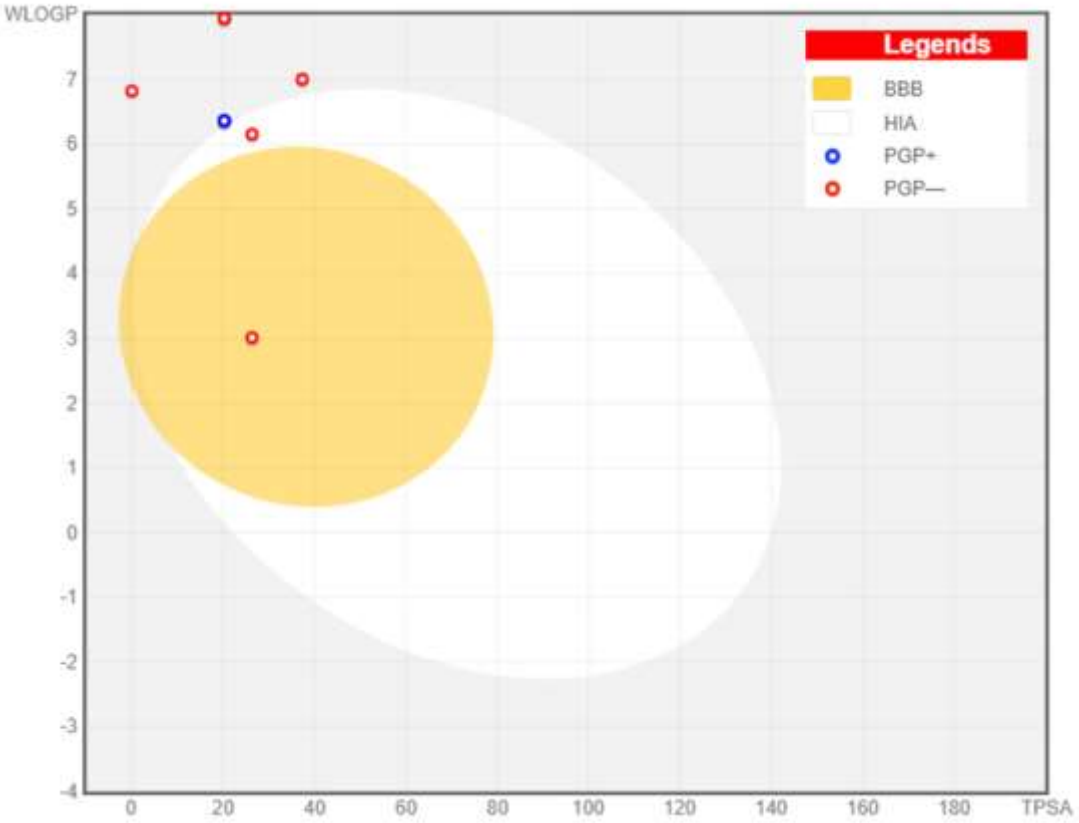


Figure 2: BIOLED-Egg illustration of bioactive compounds in MONDRP

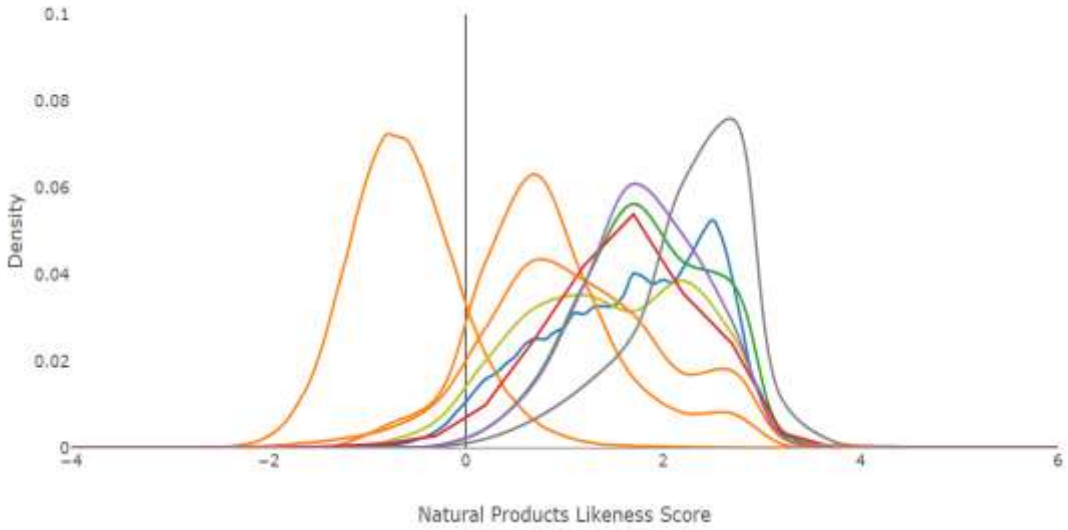
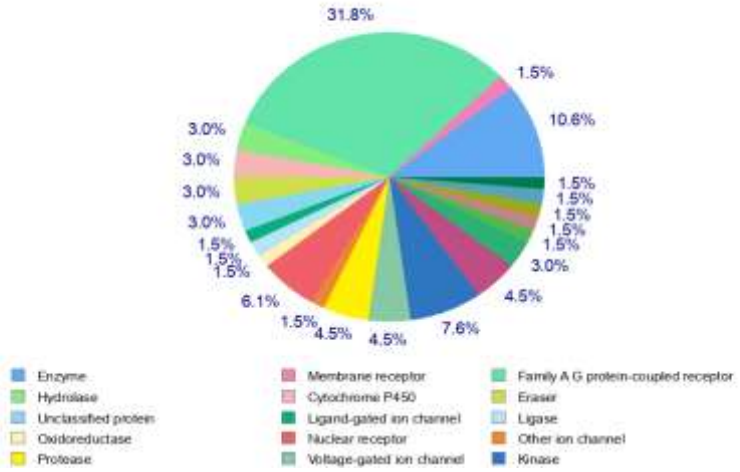
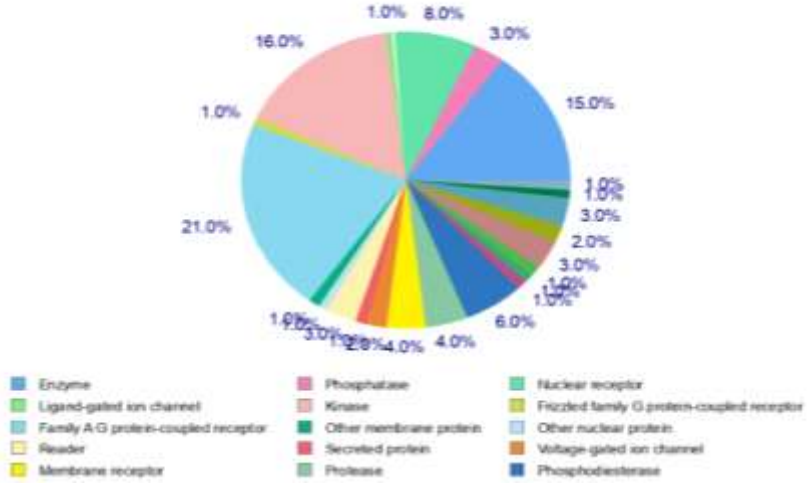


Figure 3: Natural Product Likeness Density Chart of Bioactive Compounds in MONDRP


31.8%
1.5%
10.6%
3.0%
3.0%
3.0%
3.0%
1.5%
1.5%
1.5%
6.1%
1.5%
4.5%
4.5%
7.6%
1.5%
1.5%
1.5%
1.5%
1.5%
3.0%
4.5%
Enzyme
Membrane receptor
Family A G protein-coupled receptor
Hydrolase
Cytochrome P450
Eraser
Unclassified protein
Ligand-gated ion channel
Ligase
Oxidoreductase
Nuclear receptor
Other ion channel
Protease
Voltage-gated ion channel
Kinase

a)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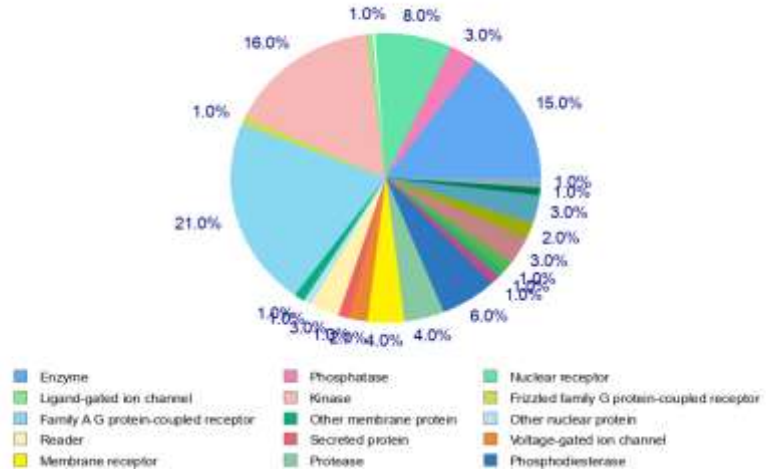
Enzyme
Phosphatase
Nuclear receptor
Ligand-gated ion channel
Kinase
Frizzled family G protein-coupled receptor
Family A G protein-coupled receptor
Other membrane protein
Other nuclear protein
Reader
Secreted protein
Voltage-gated ion channel
Membrane receptor
Protease
Phosphodiesterase

b)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Enzyme
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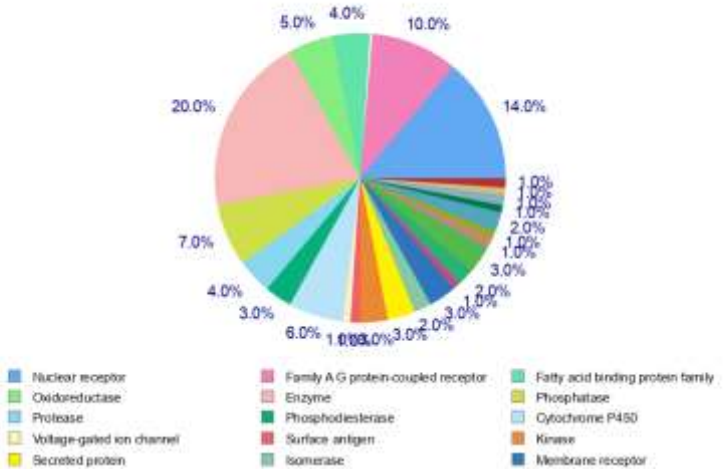
Nuclear receptor
Ligand-gated ion channel
Kinase
Frizzled family G protein-coupled receptor
Family A G protein-coupled receptor
Other membrane protein
Other nuclear protein
Reader
Secreted protein
Voltage-gated ion channel
Membrane receptor
Protease
Phosphodiesterase

c)

d)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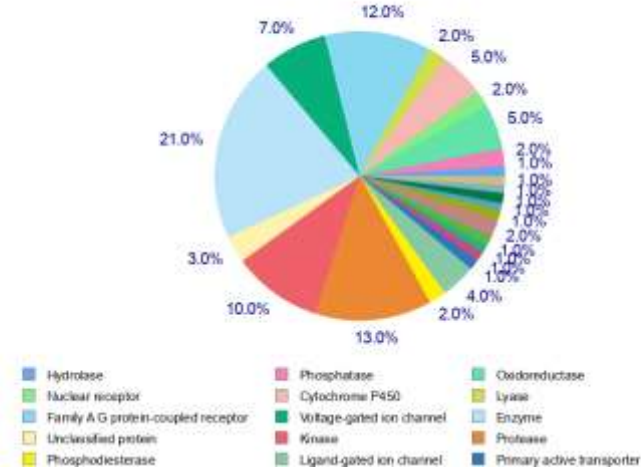
Nuclear receptor
Family A G protein-coupled receptor
Fatty acid binding protein family
Oxidoreductase
Enzyme
Phosphatase
Protease
Phosphodiesterase
Cytochrome P450
Voltage-gated ion channel
Surface antigen
Kinase
Secreted protein
Isomerase
Membrane receptor

e)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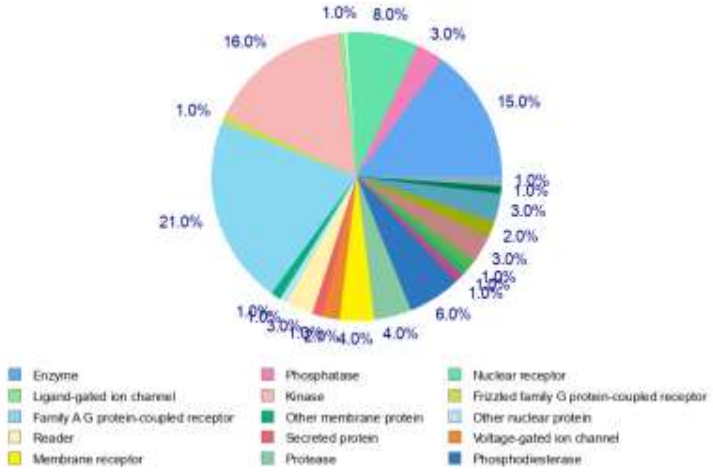
Hydrolase
Phosphatase
Oxidoreductase
Nuclear receptor
Cytochrome P450
Lyase
Family A G protein-coupled receptor
Voltage-gated ion channel
Enzyme
Unclassified protein
Kinase
Protease
Phosphodiesterase
Ligand-gated ion channel
Primary active transporter

f)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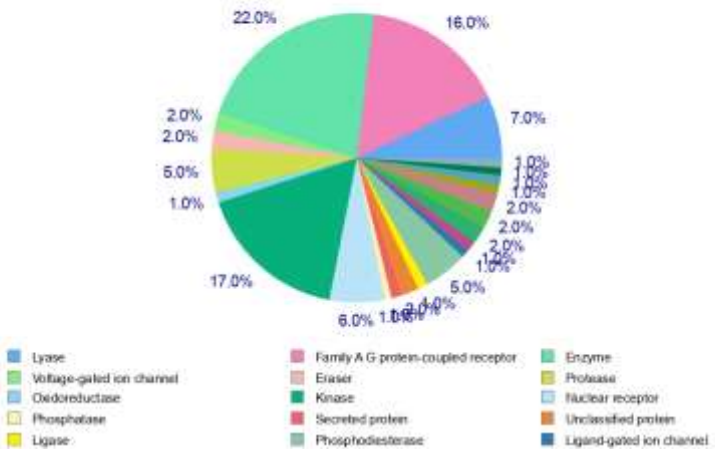
Enzyme
Phosphatase
Nuclear receptor
Ligand-gated ion channel
Kinase
Frizzled family G protein-coupled receptor
Family A G protein-coupled receptor
Other membrane protein
Other nuclear protein
Reader
Secreted protein
Voltage-gated ion channel
Membrane receptor
Protease
Phosphodiesterase

g)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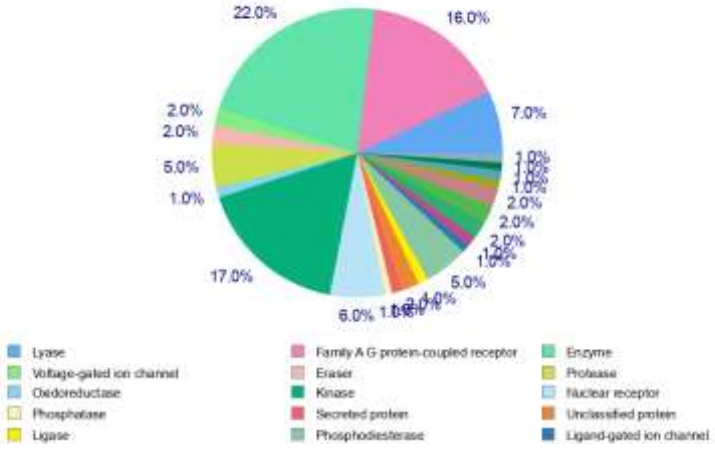
Lyase
Voltage-gated ion channel
Oxidoreductase
Phosphatase
Ligase
Family A G protein-coupled receptor
Eraser
Kinase
Secreted protein
Phosphodiesterase
Enzyme
Protease
Nuclear receptor
Unclassified protein
Ligand-gated ion channel

h)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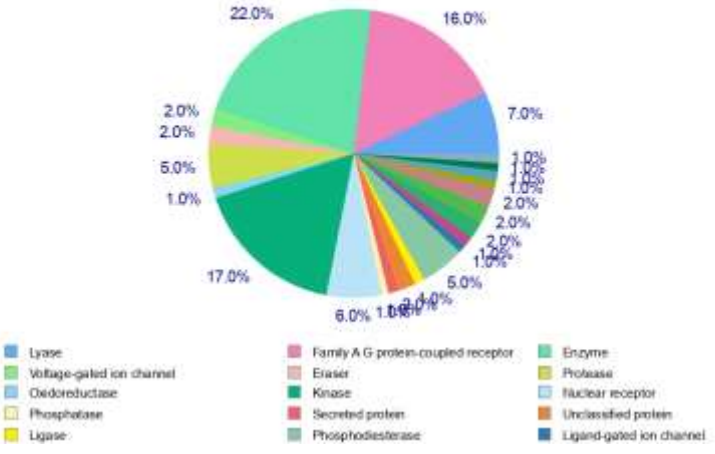
Lyase
Voltage-gated ion channel
Oxidoreductase
Phosphatase
Ligase
Family A G protein-coupled receptor
Eraser
Kinase
Secreted protein
Phosphodiesterase
Enzyme
Protease
Nuclear receptor
Unclassified protein
Ligand-gated ion channel

i)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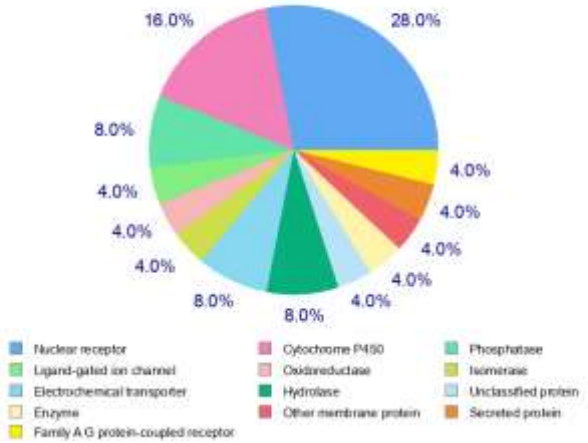
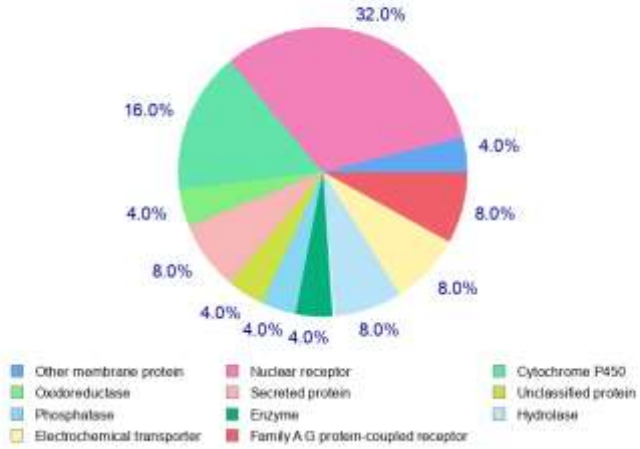
Lyase
Voltage-gated ion channel
Oxidoreductase
Phosphatase
Ligase
Family A G protein-coupled receptor
Eraser
Kinase
Secreted protein
Phosphodiesterase
Enzyme
Protease
Nuclear receptor
Unclassified protein
Ligand-gated ion channel

j)



k)



l)

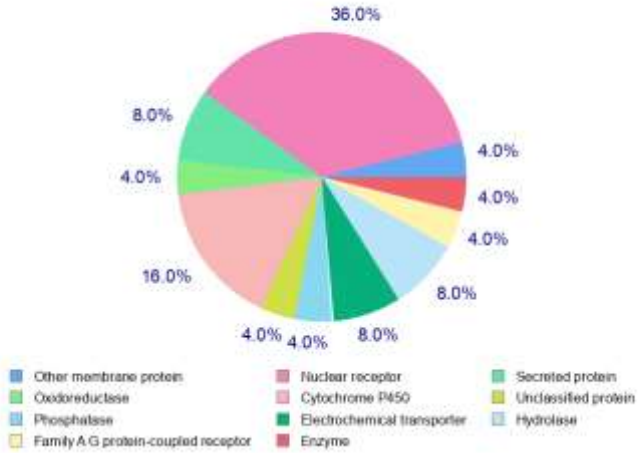


Figure 4(a-l): Swiss Target Prediction and Distribution Chart of Bioactive Compounds in MONDRP