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Annual advances of integrative pharmacology in 2018

Ke-Wu Zeng[1]*

[1]State Key Laboratory of Natural and Biomimetic Drugs, School of Pharmaceutical Sciences, Peking University, Beijing, China.

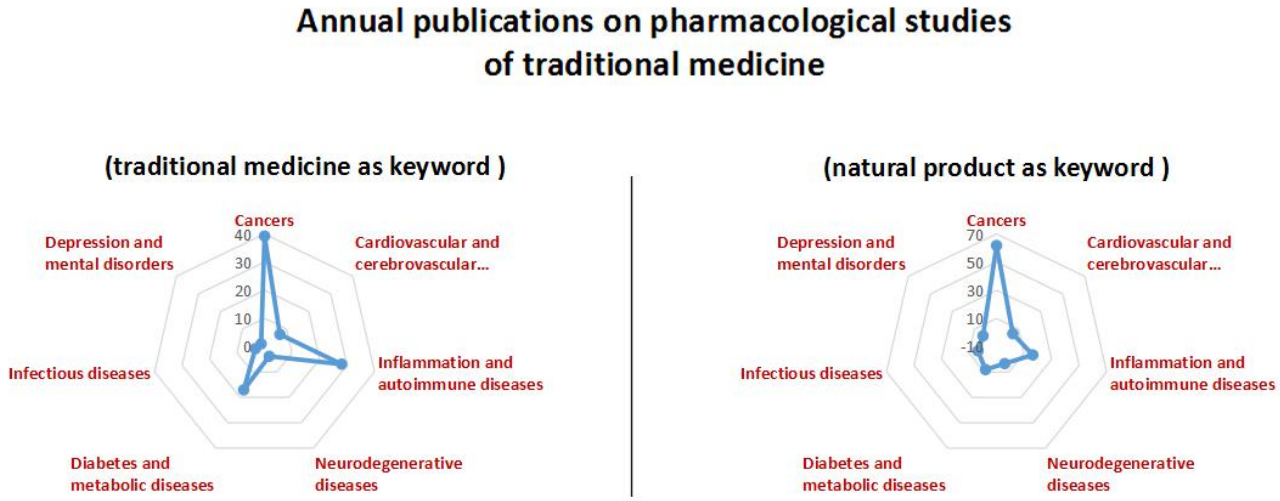
***Corresponding to:** Ke-Wu Zeng, State Key Laboratory of Natural and Biomimetic Drugs, School of Pharmaceutical Sciences, Peking University, No. 38, Xueyuan Road, Haidian District, Beijing, China. E-mail: ZKW@bjmu.edu.cn.

Highlights

This review covers the research progress during 2018 for pharmacological studies on traditional medicine and active natural products. The pharmacological reports on traditional medicine against cancers and diabetes were still hot issues.

Traditionality

This annual integrative pharmacology review analyzed the different growth rates and progress of traditional medicine in different diseases, which is able to provide a comprehensive description of the hot spot and development.



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Abstract

A number of researches concerning pharmacology of traditional medicine and active natural products over the past 12 months have outlined the importance of reviewing the progress. This annual integrative pharmacology review evaluates researches published during 2018 in different diseases including cardiovascular and cerebrovascular diseases, cancers, diabetes and metabolic diseases, and so on. The emphasis is on bioactive compounds and extracts from traditional herbs, as well as the novel molecular targets and mechanisms. Moreover, some traditional prescriptions in China and other geographical locations have also been included.
Keywords: Traditional medicine, Natural product, Herb, Cancer, Inflammation, Cardiovascular diseases

Abbreviations:

ROS, Reactive oxygen species; Nrf2, Nuclear erythroid 2-related factor 2; PPAR-γ, Peroxisome proliferator-activated receptor gamma.

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Competing interests:

There are no conflicts of interest to declare.

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Background

Giving a broad annual overview of the trend of pharmacological researches in 2018 on traditional medicine, a distinctive feature was the total amount of studies highly increased; however, the growth rates in each research area slightly differed. First, the pharmacological reports on traditional medicine against cancers and diabetes were still hot issues, and constituted the major growth points during this year. A key reason may be the direct relationships of these diseases with the aging of the social population and life-style changes. Thus, some countries with long history of traditional medicine, China in particular, have paid more and more attentions to traditional medicine studies, further promoting a rapid upsurge in this field. Statistical analysis of annual publications on pharmacological studies on traditional medicine by relative percentages on different countries was showed in figure 1. In addition, the total number of researches on cardiovascular and cerebrovascular diseases remained steady. The therapeutic agents from traditional medicine against neurodegenerative diseases attracted more and more attentions from the public, in particular for Alzheimer disease and Parkinson disease. The studies for infectious diseases with traditional medicine have become another frontier, which may be connected with the recent constant influenza virus outbreak and the increasing number of people infected with HIV. Meanwhile, there was still great room for the development of traditional medicine against depression and mental disorders.

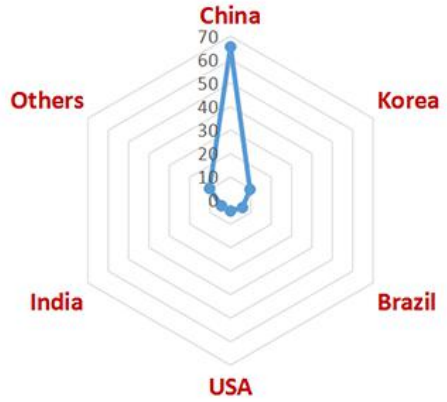

Figure 1 Statistical analysis of annual publications on pharmacological studies on traditional medicine by relative percentages on different countries

Cancers

The anti-cancer investigation based on traditional medicine still dominates a major current situation. During the whole year in 2018, a large number of studies have been reported to show versatile anti-cancer activities covering different molecular structures. Natural saponin ophiopogonin D has been reported to block lung cancer cell proliferation by inhibiting NF-κB, PI3K/Akt and AP-1 pathways [1]. Hederagenin saponin showed anti-breast cancer effect by reducing mitochondrial Apaf-1 and cytochrome c to suppress caspase-9/-3 apoptosis signal pathway [2]. Sulforaphene from *Raphanus sativus* was found to selectively inhibit lymphoma cells by activating mitophagy and apoptosis [3]. Also, alantolactone from *Inula helenium* exerted anti-pancreatic cancer effect by regulating autophagy-lysosome pathway via targeting transcription factor EB [4]. Moreover, derivatives of alkaloid tetrandrine from *Stephania tetrandra* have been found to show anti-leukemia, melanoma and breast cancer activities by activating pro-apoptotic protein Bax and blocking anti-apoptosis proteins such as survivin and Bcl-2 [5]. New anti-cancer mechanism of berberine was reported to induce cell cycle arrest in hepatocellular carcinoma cells by targeting Akt/FoxO3a/Skp2 pathway [6].

It is noteworthy that the studies on anti-cancer natural terpenoids have obviously increased. Raddeanin A triterpenoid from *Anemone raddeana* Regel was found to exert therapeutic effects on osteosarcoma [7]. (-)-trachelogenin from *Combretum fruticosum* has been reported to show anti-tumor activities on SF-295 and HL-60 cells by inducing autophagic cell death [8]. Toosendanin has been found to induce gastric cancer cell cycle G(1)/S arrest via activation of p38 MAPK pathway [9]. In addition, toosendanin, a triterpenoid from *Melia toosendan* Sieb et Zucc, showed inhibitory effect on breast cancer resistance by suppressing PI3K catalytic subunits P110α and P110β expressions [10]. Sesquiterpene curcumol from *Curcuma zedoary* effectively inhibited nasopharyngeal carcinoma NP69 cells by inducing a degradation of nucleolin protein [11]. Furthermore, some other natural compounds with distinctive structures have been reported. Flavonoid baicalin was shown to induce colon cancer cells apoptosis through decreasing c-Myc expression [12]. Lignan magnolin from *Magnolia biondii* significantly promoted apoptosis on colorectal cancer cells by targeting LIF/Stat3/Mcl-1 axis [13]. Oblongifolin C from *Garcinia yunnanensis* significantly induced pancreatic cancer apoptosis by mediating Src/MAPK/ERK pathway [14]. Notably, the polysaccharide from *Acanthopanax senticosus* exerted a marked inhibitory effect on S180, H22 and U14 solid tumors by increasing serum interferon-γ level [15], indicating a potential application of natural polysaccharide for

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anti-cancer agent development. Berbamine from *Berberis amurensis* Rupr. has been also been reported to show anti-breast cancer activities by inhibiting autophagosome-lysosome fusion [16].

Additionally, synergistic effects of different natural products were also explored. Co-treatment of arsenic trioxide with resveratrol was reported to exert a more obvious effect than single treatment against neuroblastoma [17]. Synergic action of proanthocyanidins and resveratrol on inhibiting breast cancer cells has been reported via apoptosis induction, DNA methylation and histone modifications [18]. Tanshinone IIA is a crucial natural product from traditional Chinese medicine *Salvia miltiorrhiza* Bunge. Current research revealed that tanshinone IIA could block total protein kinase C activity and selectively suppress protein kinase C isoforms ζ and ε, further leading to the synergistic antitumor efficacy with the Hsp90 inhibitors [19].

Herbal extract is also a focus of anti-cancer pharmacological investigations with traditional medicine. Graviola from *Annona muricata* was shown to exert anti-proliferative and pro-apoptotic effects in non-melanoma skin cancers by inducing G0/G1 cell cycle arrest and blocking hedgehog pathway including Smo, Gli 1/2 and Shh [20]. *Ocimum basilicum* extract inhibited the MCF7 cell proliferation and metabolism by regulating mTOR/Akt/p70S6K pathway, indicating a promising effect against the human breast cancer [21]. *Asteriscus graveolens* extract sensitized BS-24-1 lymphoma cells to chemotherapy drugs including cisplatin, etoposide and doxorubicin by increasing reactive oxygen species (ROS) level and activating caspase-3 apoptosis pathway [22]. *Kalanchoe flammea* extract showed cytotoxic effect on prostate cells by promoting phosphatidylserine translocation, ROS production, cytochrome C release and caspase-3/-9 activation [23]. The extract of *Artemisia capillaris* has been proven to inhibit the proliferation of hepatocellular carcinoma cells by down-regulation of X-linked inhibitor of apoptosis protein and promotion of cytochrome c release through PI3K/Akt pathway [24]. Chinese bayberry leaves flavonoids containing myricitrin and quercetrin inhibited ovarian cancer cell growth by inducing G1 cycle arrest and apoptosis via ERK-dependent caspase-9 apoptotic pathway [25]. The extract of *Semecarpus parvifolia* Thw. leaves exhibited significant inhibitory effect on HEp-2 cell proliferation and induced apoptosis via NO-dependent pathway [26]. Furthermore, Chinese medicine Aidi injection significantly inhibited esophageal squamous cell carcinoma metastasis by down-regulating vimentin and vascular endothelial growth factor expressions, and increasing cadherin-1 expression [27]. Taken together, these studies suggested a fine perspective for future innovative agent research from traditional medicine against cancers.

Cardiovascular and cerebrovascular diseases

Recently, the increasing risks of cardiovascular and cerebrovascular diseases in individuals are attracting great attentions. Therefore, to explore potential therapeutic strategies and agents, traditional medicine is becoming a hot topic. In the year of 2018, many studies were carried out to clarify the novel natural compounds from herbs and their pharmacological mechanisms. For instance, salvianolic acid B from *Salvia miltiorrhiza* has been found to show neuroprotective effect by targeting Nrf2- and SIRT1-dependent pathways [28]. Cucurbitacin I showed protective effect on H9c2 cardiomyoblasts from oxidative stress through regulation of mitochondrial and MAPK proteins [29]. Natural phenol phloretin showed inhibitory effect on cardiomyocyte oxidation and fibrosis by targeting Keap1/Nrf2 pathway [30]. Also, the protective effect of natural product rosamultin on H9c2 cardiomyocytes was explored. The observation showed that rosamultin effectively increased superoxide dismutase, catalase and glutathione peroxidase activities, induced Bcl-2 and phosphorylated CryAB expressions, and inhibited Bax and caspase-3/-9 expressions, indicating a promising agent for myocardial protection [31].

Moreover, some extracts from medicinal plants have been found to show potential therapeutic effects on cardiovascular and cerebrovascular system. *Urtica dioica* L. extract was found to suppress blood pressure, increase plasma antioxidant capacity and reduce systemic oxidative stress through up-regulating superoxide dismutase and catalase [32]. Other research revealed that crude methanol extract of *Rumex acetosa* exerted antihypertensive potential by inducing endothelium-dependent vasorelaxation [33]. *Eisenia bicyclis* (brown alga) extract has been reported to inhibit platelet aggregation and clot retraction by targeting P2Y12 receptor-associated signaling pathway, suggesting an anti-platelet and anti-thrombotic effect for cardiovascular diseases [34].

Additionally, some other studies focused on traditional medicine prescriptions. For example, Yangxinshi tablet exerted effective treatment for heart failure and myocardial infarction by targeting 34 proteins and 28 related pathways in immune and cardiovascular system [35]. Er-Xian decoction was proven to be effective to exert myocardial protective effect by decreasing cardiac myosin and integrin expressions [36]. Notably, Eerdun Wurile, a traditional Mongolian medicine, was found to show potential therapeutic effect on neurological deficits and regional cerebral blood circulation by increasing insulin-like growth factor I/2 expressions and inducing microglia polarization [37]. These reports indicated that the pharmacological explorations in cardio-cerebrovascular pharmacology will continue as an important traditional medicine research field.

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Inflammation and autoimmune diseases

Currently, traditional medicine has been investigated as promising approaches to inflammation and autoimmune diseases. Many natural compounds from herbs have been reported to exert obvious therapeutic effects in several inflammation-associated pathological processes. For example, berberine could significantly improve ulcerative colitis by regulating the T regulatory cell/T helper 17 cells balance against dextran sulfate sodium stimulation [38]. Smiglaside A, a phenylpropanoid glycoside from *Smilax riparia* exerted anti-inflammation effect by promoting macrophage polarization to M2 phenotype via stimulating AMPK-PPARγ pathway [39]. A derivative of danshensu effectively inhibited acute pancreatitis by blocking NF-κB, Stat3 and NLRP3 inflammasome pathways [40]. O-orsellinaldehyde from *Grifola frondosa* has been reported to show anti-inflammatory and pro-apoptotic effects by targeting NF-κB kinase β [41]. Additionally, artemether attenuates inflammatory bone loss by inhibiting receptor activator of nuclear factor-κ B ligand-induced MAPKs activity [42]. Natural product capnoidine from *Corydalis dubia* can effective inhibit mouse colitis model by down-regulating p-IκB (Ser32) and p-NF-κB p65 (Ser536) levels [43]. Falcarinol from *Notopterygium incisum* inhibited intestinal inflammation by inducing heme oxygenase-1 expression [44]. Henceforth, extensive researches on anti-inflammation agents from traditional medicine will continue in the future.

The therapeutic effect of sesquiterpene lactones from *Inula helenium* L. on atopic dermatitis has been investigated. The sesquiterpene lactones could markedly reduce epidermis thickening and inflammatory infiltration by suppressing NF-κB activation and decreasing the expressions of tumor necrosis factor-α, IL-1 and IL-4 [45]. Total flavonoids from Radix *Glycyrrhiza* showed marked anti-inflammatory effect via mediating ERK/NF-κB/miR-155 pathway to suppress inducible nitric oxide synthase expression [46]. Furthermore, *Terminalia coriacea* extract significantly decreased paw volume as well as wet and dry weights of cotton pellets in acute and chronic inflammatory models [47]. *Terminalia bellirica* extract and ellagic acid showed anti-inflammation effect through regulating MAPK/NF-κB and Akt/AMPK/Nrf2 pathways [48]. Notably, Sanmiao Wan together with berberine has been found to show better therapeutic effect than Sanmiao Wan alone on knee joint swelling and synovial hyperplasia of acute gouty arthritis rats, by decreasing the multidrug resistance protein 1 and P-glycoprotein expressions [49]. Collectively, these findings indicated a great opportunity for anti-inflammation and autoimmune agent development from traditional herbal extracts and prescriptions.

Neurodegenerative diseases

In the year 2018, the explorations for novel neuroprotective agents continued unabated, due to the trend of the modern ageing population. Thus, the number of reports on pharmacological mechanism studies on traditional neuroprotective medicine has increased somewhat. The neuroprotective effect of rhynchophylline from *Uncaria rhynchophylla* was found to inhibit 1-methyl-4-phenylpyridinium ion -induced neuronal injury by activating myocyte enhancer factor 2D via PI3K/Akt/GSK3β pathway [50]. Isocoumarin was reported to activate tropomyosin-related kinase B receptor and improve synaptic plasticity in neurons, indicating a promising potential in neuroprotection [51]. Natural product methyl salicylate lactoside showed therapeutic effect on cognitive preservation by regulating neuronal mitochondrial function and oxidative stress via inhibiting JNK and p38 MAPKs phosphorylation and cyclooxygenase-1/2 expressions [52]. *Codonopsis pilosula* polysaccharides could suppress tau hyperphosphorylation by inducing protein phosphatase 2A activity and restoring synaptic plasticity and synaptogenesis, indicating a promising effect for tau pathology in Alzheimer's disease [53].

Moreover, some single Chinese herbs or extracts have attracted more and more attentions. Traditional herb *Apium graveolens* L. has been reported to exert neuroprotective effects against Parkinson's disease through regulation of neurotransmitter pathways and up-regulation of dopaminergic neurons number [54]. *Acanthus ebracteatus* extract was found to exert neuroprotective effect in glutamate-induced hippocampal cells by suppressing apoptosis-inducing factor nuclear translocation and up-regulation of nuclear erythroid 2-related factor 2 (Nrf2) [55]. Guarana hydroalcoholic extract could inhibit polyglutamine protein aggregation, decrease neuronal death and improve β-amyloid-induced paralysis, indicating a potential therapeutic effect in age-related diseases [56]. Meanwhile, traditional prescriptions are important sources of neuroprotective agent development too. For example, Sagunja-tang fermented with lactobacillus strains showed a more obvious neuroprotective effect on H_2O_2 and etoposide-induced SH-SY5Y cells by inhibiting ROS production and decreasing mitochondrial membrane potential [57]. The therapeutic effect of Huatuo Zaizao pill could suppress memory deficits and improve synaptic functions through blocking amyloid plaque deposition by targeting α- and γ-secretase [58]. Therefore, there will be a stirring of interest in further researches on prescriptions for neurodegenerative diseases.

Diabetes and metabolic diseases

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Metabolic diseases are attracting more and more attentions during these years. Therefore, an increasing number of studies on anti-diabetes agent developments from traditional medicine have been reported. Several compounds from traditional herbs with different structural types have been reported to show therapeutic effects on metabolic disorders. Halimane-type diterpenoids from traditional herb *Vitex rotundifolia* have been reported to exert anti-hyperlipidemia activity by promoting low-density lipoprotein uptake [59]. Pentacyclic triterpenes from *Cecropia telenitida* exerted a significant hypoglycemic effect in an insulin-resistant murine model by inhibiting 11-hydroxysteroid dehydrogenase type 1 enzyme activity [60]. Also, breviscapin, mangiferin and mangostin derivatives were reported to show improvement effects on treating type 2 diabetes by inhibiting dipeptidyl peptidase-IV [61]. Puerarin inhibited liver injury in type 2 diabetic rat model through suppressing NF-κB-dependent proinflammatory cytokines expressions via TGF-β/Smad signaling pathway [62]. *Sophora japonica* L. is a traditional Chinese herb rich in sophoricoside. Current study showed that sophoricoside could markedly decrease liver weight and down-regulate the hepatic cholesterol and triglyceride levels. Moreover, sophoricoside effectively decreased serum low density lipoprotein-cholesterol level, indicating a promising agent for liver injury [63]. Sanbai melon seed oil showed obvious therapeutic effect on weight loss, polydipsia, and plasma insulin/lipid levels by regulating estrogen receptor and mitochondrial dependent signaling pathways [64]. Polysaccharides from Chinese Liupao dark tea has been reported to show hypolipidemic effect through improving the levels of lipid profiles, the oxidation of lipids and antioxidant enzyme activity [65].

The herbal extract is also an important point of concern. The extract from *Myrianthus arboreus* exerted significant anti-diabetic effect by regulating hepatocyte glucose homeostasis [66]. *Dendrobium* extract obviously decreased the fasting blood glucose and blood lipids in diabetic rats, and also improved insulin resistance, through regulating PI3K/Akt signaling pathway [67]. The extract of chicory root rich in chicoric acid significantly improved glucose tolerance and the basal hyperglycemia in streptozotocin-induced diabetic rats [68]. *Moringa concanensis* Nimmo ethanolic extract has been reported to exert antidiabetic effect by regulating lipid accumulation, inducing expressions of peroxisome proliferator-activated receptor gamma (PPAR-γ), C/EBP-α and adipogenin via Akt pathway [69]. *Ligusticum chuanxiong* extract was shown to inhibit streptozotocin-induced urine production, urinary albumin excretion and urine albumin-to-creatinine ratio by targeting Nrf2 and NF-κB signaling pathways [70]. *Garcinia cambogia* and pear pomace extracts have been reported to inhibit adipocyte differentiation by targeting adipogenic transcription factor CCAAT/enhancer binding protein and PPAR-γ, suggesting a potential therapeutic effect for obesity-related diseases [71].

Additionally, herbal prescription such as MD-1 (a poly herbal formulation is constituted as a mixture of six popular anti diabetic herbs), which was traditionally used for diabetes mellitus, has been found to improve glucose uptake and insulin sensitivity by targeting PPAR-γ agonism [72]. Huangkui capsule, a Chinese modern patent medicine, improved body weight, serum albumin, kidney weight and hypertrophy index by suppressing Akt/mTOR/p70S6K signaling pathway [73]. Jiang Zhi Granule is an herbal prescription for non-alcoholic fatty liver disease. Jiang Zhi Granule was found to show therapeutic effect on hepatic dysfunction and lipid droplet accumulation by inducing lipid droplet degradation though mTOR pathway [74]. Xiao-Shen-Formula is an herbal prescription for renal injury in type 1 diabetic nephropathy. The protective effect of Xiao-Shen-Formula may be resulted from vascular prevention and anti-inflammation by interacting with multiple pharmacological targets [75]. Therefore, the multicomponent characteristics of herbal prescriptions may exactly agree with the multigene pathology of diabetes and metabolic diseases, representing a promising development direction in the future for new drug discovery.

Infectious diseases

There is also an obvious increase in the number of reports on anti-infectious herbal agents since 2018. Infectious diseases especially for malaria, viruses and fungus can cause many different symptoms to human health. Thus, active explorations on these novel anti-infectious agents from traditional medicine have become a hot research area. For instance, curcumin showed therapeutic effect on HBV infection by regulating NF-κB, AP1 and Wnt/β-catenin signaling pathways [76]. Some anti-malarial natural compounds and extracts have been screened and berberine chloride, coptisine chloride, palmatine chloride, and dehydrocorydaline nitrate were found to exert well anti-malarial effects with low cytotoxicity. Additionally, *Phellodendri cortex* and *Coptidis rhizome* extracts were found to show strong antiplasmodial effects [77]. Tea polyphenol proanthocyanidin A2 has been reported to show anti-viral activity against porcine reproductive and respiratory syndrome virus infection by inhibiting viral RNA synthesis, protein expression and progeny virus production [78]. Psoralen and angelicin from traditional herb psoraleae, were reported to effectively inhibit *Porphyromonas gingivalis*, and decrease the release of inflammatory mediators, indicating a potential therapeutic effect against periodontitis [79].

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The herbal extracts for infectious diseases have also drawn enough attentions. The extract from herb *Aspidosperma pyrifolium* showed obvious anti-malarial effect *in vivo* [80]. *Poncirus trifoliate* extract was found to markedly inhibit influenza viruses activity via targeting the cellular penetration pathway [81]. *Cranberry* extract was shown to block the replication of influenza A and B viruses via inhibition of the attachment and entry of influenza viruses into target cells, indicating cranberry extract may act as a potential agent for antiviral activity [82]. Moreover, polar *Origanum vulgare* extract has been reported to show antifungal activity against *Sporothrix brasiliensis*, for a potential use for clinical sporotrichosis [83]. *Hypericum* extract, which has been traditionally used for the treatment of respiratory infections, were found to show broad-spectrum antifungal activity such as *Penicillium* and *Aspergillus* [84]. *Trapa natans* L. extract and active compounds including ellagic and ferulic acids were found to interfere with *Pseudomonas aeruginosa*, suggesting an anti-virulence effect against microbial infections [85]. *Polygonum ciliinerve* was reported to exert therapeutic effect against *Staphylococcus aureus* infections, indicating a potential application for pneumonia treatment [86]. Therefore, the current enthusiasm for the development of anti-infectious agents against sensitive bacteria, viruses and fungus will still maintain.

Depression and mental disorders

Great progress in traditional medicine on mental diseases has not been well made in this year. However, there were still some inspiring work can be addressed. Phenolic compound gastrodigenin from *Gastrodia elata* has been reported to show anti-depressant effect through regulating monoaminergic system, GABAergic system and BDNF/TrkB signaling pathways, indicating a promising perspective in the future [87]. Moreover, the linalool-rich essential oils from the leaves of *Aniba rosaeodora*, *Aniba parviflora* and *Aeollanthus suaveolens* exerted significant anti-depressant effect in rodents [88]. *Fraxinus rhynchophylla* Hance extract also effectively improved chronic stress-induced behaviors in the open field and forced swim tests by activating pCREB/BDNF signaling pathway and inhibiting neuroinflammation progress [89]. In-depth research work should be promoted to explore the detailed molecular mechanism for neurotransmitter regulation as well as seeking more potential herbal extracts and compounds for depression and mental disorders in the future.

Other diseases

In addition to the above-mentioned studies, there are some other research hotspots worth attention. Chronic hepatic injury resulted from excessive drinking or overweight is an urgent problem in modern society. Baicalin, a flavonoid from *Scutellaria baicalensis*, has been found to treat hepatic steatosis via directly targeting carnitine palmitoyltransferase 1 [90]. Dioscin from *Rhizoma dioscoreae* showed potential therapeutic effect against non-alcoholic fatty liver via SIRT1/AMPK signal pathway [91]. *Hemerocallis citrina* extract has been found to inhibit BRL-3A cells apoptosis by inducing the expressions of AMP-activated protein kinase, extracellular signal-regulated kinase/p38, MAPKs, Nrf2, superoxide dismutase and heme oxygenase 1, indicating a potential hepatoprotective effect [92]. Moreover, Yiguanjian decoction was reported to promote fetal liver stem/progenitor cells-dependent repair of liver cirrhosis through regulation of macrophage activation via canonical and non-canonical Wnt signaling pathways [93].

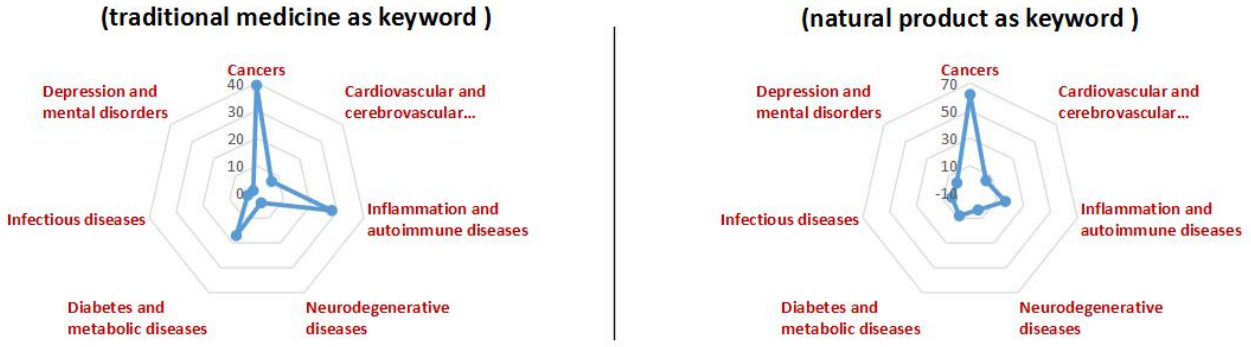

Figure 2 Statistical analysis of annual publications on pharmacological studies on traditional medicine by relative percentages on different diseases

It is also worth mentioning that, Bixin from *Bixa*

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orellana protected PM2.5 particles-induced lung injury via Nrf2 pathway [94]. Tart cherry showed a therapeutic effect in bone stiffness by inhibiting RANKL pathway [95]. Essential oil from *Eugenia dysenterica* significantly induced skin cell migration to promote damaged tissue repair and wound healing [96]. Notably, the enriching-blood effects of several kinds of *Angelica sinensis* were investigated and reported [97]. The extract of *Rhynchosia volubilis* Lour. could effectively protect the cornea of mouse dry eye model induced by benzalkonium chloride, indicating a potential application for dry eye disease [98]. Also, the phenolic compounds from *Vaccinium angustifolium* effectively promoted trophoblast migration and invasion via adenosine monophosphate-activated protein kinase-dependent mechanism [99].

Conclusion

Taken together, the annual researches showed a variety of characteristics, and the fields of pharmacological explorations with traditional medicine have covered current major diseases (Figure 2). However, the studies mainly focused on the elucidation of pharmacological mechanisms of the compounds and crude extracts from traditional medicine. A possible reason for the scarce pharmacological reports on standard herbal extracts may be the instability and inhomogeneity of chemical constituents, further causing the non-repeatability of experiments. Therefore, different labs between analytical chemistry, pharmacology and translational medicine should try to cooperate together to solve these problems. What is worth mentioning is the increasing number of the researches on traditional prescriptions this year; however the molecular mechanisms investigations are still not enough. Especially, the pharmacological targets identification of complex system remains to be the most severe challenge in the future.

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