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Perspectives, Experiences, and Practices of Healthcare Professionals and Patients Towards Herb–Drug Interaction: A Systematic Review of Qualitative Studies

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ABSTRACT

The aim of the study was to understand healthcare professionals, pharmacists, and patients perspectives and experiences on clinical practice of herb–drug interactions (HDIs). A systematic review of qualitative studies was conducted. 10 electronic databases were searched from inception through September 2023. Qualitative studies, mixed-method studies, and unstructured or semi-structured cross-sectional surveys focused on healthcare professionals, pharmacists and patients' perspectives, attitudes, clinical practice behaviors, and information needs regarding HDI were included. Thematic synthesis employed Nvivo 12 software. Of 6655 studies identified, 1267 full-text articles were retrieved. Of these, 18 studies conducted in 11 countries/regions were eligible for inclusion, involving 1273 patients, 302 healthcare professionals, and 230 pharmacists. Five over-arching explanatory themes were identified: perspectives, attitudes, practices, experiences, expectations, and information needs. Complementary and alternative (CAM) physicians, pharmacists, and general practitioners were considered by patients to possess the ability or responsibility to assess potential HDIs. Pharmacists yet encountered difficulties due to conflicting information sources and inadequate training. Healthcare professionals, including pharmacists, usually only assessed HDIs when they were deemed to cause serious adverse effects. Regarding expectations and information needs, patients were particularly concerned about the risk of adverse HDIs, the severity of HDIs, and the appropriate intervals between drug doses. They would like to receive relevant HDI alerts. Results suggest that government, policy makers, healthcare professionals, and the education system should give attention to HDIs and improve health professional–patient communication. Further research should also be conducted on the understanding and practices of CAM practitioners in China.

Trial Registration: CRD42022324777 (<https://www.crd.york.ac.uk/PROSPERO/#recordDetails>)

Abbreviations: CAM, Complementary and alternative; DDIs, drug–drug interactions; DRPs, drug-related problems; ENTREQ, Extending Transparency in Reporting Qualitative Research; HDI, herb–drug interaction; SR, systematic review

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1 | Introduction

Herb–drug interactions (HDIs) are defined as the interplay between herbs, plants, or plant extracts and conventional drugs, affecting a drug's activity, metabolites, or toxicity (Yeung, Gubili, and Mao 2018). Among patients receiving conventional pharmacotherapy, 15% also use herbal products, with 40% experiencing potential adverse HDIs (Bush et al. 2007). In the light of the prior experience and understanding of HDIs as “potentiation and toxicity reduction” (Tian and Chen 2019), as well as the complexity of the components of herbal productions, it is essential that HDIs be assessed on both an effective and a risk basis in clinical practice (Yang, Luo, and Liu 2021).

When prescribing herbal medicines and conventional pharmacotherapies together, the following variables should be considered: indication, prescription composition, comorbidities that may affect pharmacokinetic and pharmacodynamics changes (e.g., renal, hepatic or cardiac failure, individual metabolic specificity), and potential drug–drug interactions (DDIs) (Strandell and Wahlin 2011). Complementary and alternative (CAM) practitioners, general practitioners, physicians, and pharmacists all play an important role in monitoring drug interactions and drug-related problems (DRPs), optimizing drug treatment regimens, and preventing adverse events related to medical quality and safety (Bourne, Shulman, and Jennings 2018), (Lee et al. 2017). A study in France designed and applied a pharmacist intervention form for daily use in order to standardize the recording of pharmacist interventions in the DDIs, the entries of which included monitoring of DRPs, for example, drug interactions, pharmacist interventions, types of medications involved, and follow-up of interventions (Allenet et al. 2006). HDIs, however, have not been addressed by standardized procedures or intervention forms in various countries to provide pharmacists and medical workers with guidance.

This qualitative systematic review (SR) systematically summarizes and evaluates qualitative research across different countries/regions, cultures, and methodologies. The aim of the review was to gain a better global understanding of the perspectives, experiences, and practice on HDIs among healthcare professionals, pharmacists, and patients, thereby improving the knowledge on potential HDIs occurring in practice.

2 | Methods

This study was a SR of previously published studies. The Extending Transparency in Reporting Qualitative Research (ENTREQ) guideline for transparent reporting was followed in this study (Tong et al. 2012).

2.1 | Eligibility

The eligibility criteria for including studies were formulated using the SPIDER tool (Cooke, Smith, and Booth 2012). Eight authors (S.C., K.L.Y., L.H.D., R.Z.Y., W.Z.L., Y.X.L., C.P.P., and X.L.X.) conducted independent screenings of the records in pairs. The sample (S) included patients and (or) healthcare professionals such as physicians (or prescribers), pharmacists,

or nurses. The population of interest was not limited by age, gender, race, or ethnicity. The phenomenon of interest (PI) was HDI, which could encompass interactions that can enhance/reduce clinical outcomes and/or adverse reactions. Studies involving broad drug interactions were included only if they explicitly reported that the category of drug interactions includes HDIs.

The study design (D) utilizing qualitative research methods included data collection methods such as observational studies, interview studies, documentary sources, focus group/discussions, nominal group methods, consensus methods (Delphi process), (the nominal group technique (NGT) and consensus development conference), case studies, autoethnography, and patient-reported outcomes. Data analysis methods could include thematic analysis, framework analysis, discourse analysis, rhetorical analysis, grounded theory, semiotic analysis, situational analysis, and categorical analysis. We also included the open-ended response section of non-structured or semi-structured questionnaires. The evaluation (E) contents included, perspectives (understanding, opinions, etc.), attitudes, experiences (healthcare and consultation experience, medication experience, etc.), clinical practice behaviors (medication regimen, medication assessment procedures, medication counseling/guidance, patient adherence, etc.), and information needs regarding HDI. The type of research (R) included, qualitative research, mixed methods research, and cross-sectional studies. In addition, language was limited to English and Chinese languages. Exclusion criteria included incomplete or missing information in the published literature or publications limited to abstracts only.

2.2 | Search Strategy

To retrieve relevant studies, the following databases were searched from inception to September 2023: PubMed, Embase, Web of Science (SSCI), Campbell, ProQuest-P, Cochrane Library, China National Knowledge Infrastructure (CNKI), Wanfang Data, VIP Database, and Chinese Biomedical Database (SinoMed). We also screened the reference lists of included studies for further relevant publications. We used the following free text and MeSH terms: knowledge, perception, understanding, experience, attitude, belief, perspective, practice, behavior, prescription, medical order, communication, compatibility, pharmaceutical care, medical administration, compliance, drug interaction, drug agonism, drug partial agonism, drug antagonism, drug collateral sensitivity, drug inverse agonism, drug synergism, food–drug interactions, HDIs, qualitative research, qualitative study, phenomenology, hermeneutics, interview, focus group, observational study, qualitative case study, thematic analysis, survey, questionnaire, cross-sectional study, mix-method study, qualitative research, hermeneutics, interview, focus group, surveys and questionnaires, and cross-sectional study. As an example, the search strategy used in PubMed database can be found in Appendix 1.

2.3 | Study Selection

Following the Cochrane Handbook (v6.3.0), we conducted independent literature screening. After removing duplicates using

NoteExpress software, eight researchers (S.C., K.L.Y., L.H.D., R.Z.Y., W.Z.L., Y.X.L., C.P.P., and X.L.X.) independently screened the publications in pairs. First, the titles and abstracts were read and selected based on the eligibility criteria. The full texts of the 1st round of inclusion were then retrieved and screened for selected publications. Any discrepancies were resolved through discussion between the paired researchers. If conflict persisted, a third researcher (LJP) made the final decision.

2.4 | Data Extraction, Statistical Synthesis and Analyses

We used a standardized data extraction form pre-designed with the JBI-QARI (Joanna Briggs Institute-Qualitative Assessment and Review Instrument) and conducted data extraction of basic information of included literature using Excel 2016 software independently by six authors (S.C., K.L.Y., L.H.D., R.Z.Y., W.Z.L., Y.X.L.). The extracted data included (1) study information (study ID, title, publication year, study implementation site/setting, research purpose); (2) research methods (data collection methods, data analysis methods); (3) geographical location (country where the study was conducted); (4) specific content (start time and duration of study, drugs of interest, and diseases of interest); and (5) study participants (age, gender, cultural background, workplace, occupation, sample size).

We used a thematic synthesis approach (Thomas and Harden 2008) to synthesize the qualitative data. The full text of each study was imported into Nvivo 12 software for coding. Three coding stages were conducted: (1) line-by-line coding of study results; (2) categorizing codes into descriptive themes; (3) developing analytical themes to describe and/or explain the descriptive themes. Essential concepts related to HDIs were identified through comprehensive reading of the original research. Initial viewpoints, quotes, statements, and explanations highlighting knowledge, clinical practice, experience, or information needs were marked as raw data for qualitative synthesis and formed first-level themes. Key points were extracted and integrated, forming second-level themes. Second-level themes were then categorized into third-level themes. The first author coded the dataset and shared it with the other authors for confirmation. Double-coding and resolving discrepancies through discussions were ensured. The team collaborated to refine the final descriptive themes, analytical themes, and explanatory framework. Although healthcare professionals include pharmacists, due to the specificity of this study's topic, healthcare professionals (other than pharmacists) and pharmacists will be analyzed and described as two separate groups.

2.5 | Quality Assessment

We used the Critical Appraisal Skills Programme Qualitative Research Checklist (CASP) (Critical Appraisal Skills Programme 2018) to evaluate the methodological quality of the qualitative research, assessing the transparency of the literature included and evaluating the rigor, credibility, and relevance of the study. The evaluation criteria included study objectives, research methods, study design, research subjects, data collection, the relationship between researchers and subjects, ethical considerations, data analysis, research results, and research value. Quality

evaluation was conducted by two researchers, who evaluated each item of the quality evaluation. Both researchers reached a consensus on the final rating and provided an explanation for each item. For mixed-methods research or open-ended questionnaire responses, only the qualitative research section was evaluated.

3 | Results

3.1 | Description of Studies

As shown in Figure 1, based on electronic and manual searching, a total of 6655 citations were obtained. 18 references (Alhomoud 2014), (Christensen et al. 2017), (Dharmarajan et al. 2006), (Gokcekus et al. 2012), (Little et al. 2018), (Makkaoui et al. 2020), (Meshesha et al. 2020), (Moen et al. 2009), (Muñoz et al. 2013) (O'Callaghan and Quine 2007), (Skovgaard, Pedersen, and Verhoef 2014), (Smith et al. 2010), (Vickers, Jolly, and Greenfield 2006), (Watt et al. 2012), (Williamson and Maguire 2008) (Odegard et al. 2022) (Tsele-Tebakang, Morris-Eyton, and Pretorius 2022), (Tsele-Tebakang, Morris-Eyton, and Pretorius 2023) were included for final analysis. Among them, one was a doctoral thesis, and 17 were journal articles. All 18 references were in English.

The basic information of the included studies is shown in Table 1. The 18 studies were published between 2006 and 2023, involving 11 countries or regions. No studies were conducted in China. The data collection methods included structured/semi-structured interviews, focus group interviews, and semi-structured questionnaires and one study collected data through the participation of standardized patients in pharmacy consultation. 16 studies were conducted face to face, and two studies were conducted through online questionnaires or telephone interviews. The study included a total of 1805 participants, including 1273 patients (including parents of sick children and standardized patients), 302 healthcare professionals other than pharmacists, and 230 pharmacists. Three studies investigated herbal-related issues among immigrant populations (South Asians, Middle Easterners, Vietnamese, and Chinese) living in the UK, Australia, and Canada, while one study compared the attitudes of healthcare workers in the US-Mexico border region toward the use of CAM medicine. 10 studies mainly explored HDIs, one study explored DDIs and HDIs, and the remaining seven studies explored broad category of drug interactions, including HDI.

3.2 | Quality Assessment Results of Included Studies

The CASP evaluation results are shown in Table 2. All included studies clearly stated their objectives, methods, and results. The research design and subject recruitment strategies of the included studies aligned with their research purpose, and the data collection methods employed were effective in addressing research problems. Three studies acknowledged the potential bias associated with subject recruitment and discussed this issue. Additionally, seven studies employed convenience sampling or purposive sampling without addressing the possible bias introduced by these methods. Two studies explicitly

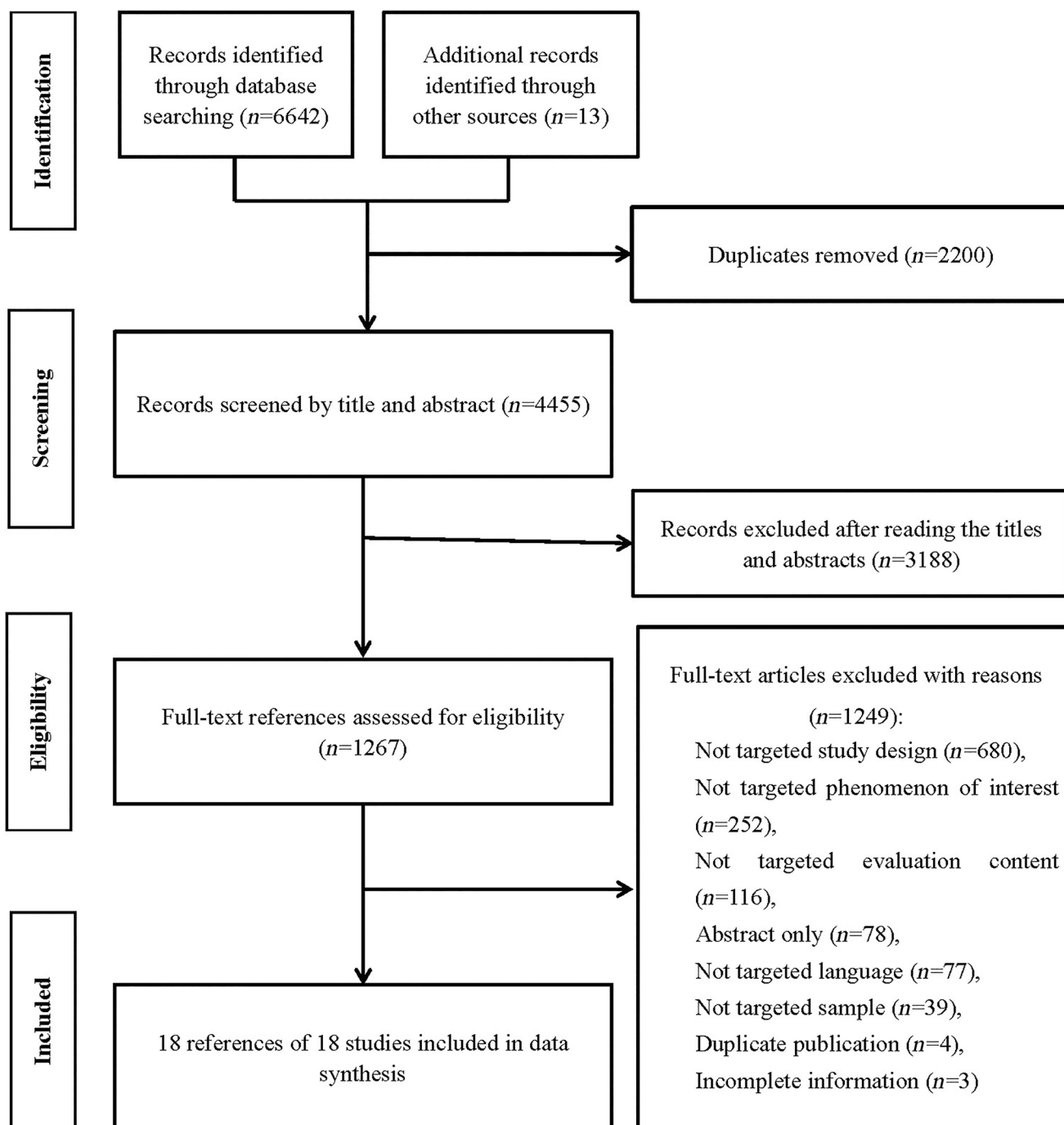


FIGURE 1 | Flow chart of literature search and selection of studies.

stated the absence of ethical approval, while four studies did not mention ethical or informed consent issues. Three studies employed semi-structured questionnaires and interviews but did not explicitly elucidate their methodology for handling qualitative data.

3.3 | Data Synthesis Results

After refining, summarizing, and integrating the included data, we formed five third-level themes: perspectives, attitudes, practices, experiences, and expectations and information needs,

which were explored around three groups of people: health-care professionals (excluding pharmacists), pharmacists, and patients. The synthesis results of the themes are detailed in Appendix 2.

3.3.1 | Perspectives

Within the perspectives theme, five main themes were identified: sources of knowledge, level of knowledge, multiple medications in combination, understanding of HDI, and roles and responsibilities. Patients' knowledge regarding HDIs came

TABLE 1 | Characteristics of included studies.

ID	Country/region of research conduct		Research duration	Research focus	Sample size	Role of participants	Participants' race or ethnicity	Data collection method	Form of data collection	Qualitative data analysis method
Alhomoud 2014	United Kingdom	2011.1–2014.6	MRPs	80	Patients	South Asian and Middle Eastern	South Asian and Middle Eastern	Semi-structured interview	Offline	Thematic framework analysis
Christensen et al. 2017	United States	NR	Needs and preferences for herb–drug–disease interaction alerts	50	Patients	Spanish American, Non-Spanish American	Spanish American, Non-Spanish American	Structured Interview	Offline	Content analysis
Dharmarajan et al. 2006	United States	NR	Decision to anticoagulate or not in older patients with dementia and atrial fibrillation	107	Physicians	NR	NR	Semi-structured questionnaire	Offline	Descriptive statistics
Gokcekus et al. 2012	Turkish Republic of Northern Cyprus	2009.3–6	Community pharmacists' dispensing practices	137	Community pharmacists	NR	NR	Semi-structured interview, simulated patients	Offline	Descriptive statistics
Little et al. 2018	United States	NR	School medication management needs of school nurses; Interprofessional collaboration between school nurses and pharmacists	155	School nurses	White, African American or Black, Asian, American Indian or Alaska Native, Pacific Islander, Hispanic, or Latino	White, African American or Black, Asian, American Indian or Alaska Native, Pacific Islander, Hispanic, or Latino	Semi-structured questionnaire	Online	Content analysis
Makkaoui et al. 2020	Lebanon	NR	KAP community pharmacists regarding drug interaction screening.	89	Community pharmacists	NR	NR	Semi-structured questionnaire and interview	Offline	NR

(Continues)

TABLE 1 | (Continued)

ID	Country/region of research conduct	Research duration	Research focus	Sample size	Role of participants	Participants' race or ethnicity	Data collection method	Form of data collection	Qualitative data analysis method
Meshesha et al. 2020	Ethiopia	2016.4–8	Magnitude of concomitant use of herbal and conventional antidiabetic medicines	791	Patients	NR	Questionnaire	Offline	Descriptive statistics
Moen et al. 2009	Sweden	2006.11–12	Multiple medicine use from the elderly patient's perspective	8	Physicians		Semi-structured interview		Content analysis
Muñoz et al. 2013	Mexico and United States	2010.7–12	Beliefs and perceptions regarding the use of CAM and the communication practices with patients.	19	Health care professionals	Mexican/ Hispanic/ Latino, non-Latino White, Korean/ Japanese, Greek	Semi-structured interview	Offline	Grounded theory
O'Callaghan and Quine 2007	Australia	Late 1999–early 2000	The impact of limited health literacy on medication management among Vietnamese Australian women.	20 20	Patients	Vietnamese Australian	Semi-structured interview Focus group interview	Offline	NR
Odegard et al. 2022	United States	NR	The perceptions of CAM among adult residents of Hawaii.	21	Patients	Asian, Native Hawaiian, Pacific Islander, African American, White, Hispanic, Not Hispanic	Semi-structured interview	Offline	Content analysis

(Continues)

TABLE 1 | (Continued)

ID	Country/region of research conduct	Research duration	Research focus	Sample size	Role of participants	Participants' race or ethnicity	Data collection method	Form of data collection	Qualitative data analysis method
Skovgaard, Pedersen, and Verhoef 2014	Denmark	NR	Perspectives on the risks of negative interactions between herbal medicine and conventional drug therapies among individuals with multiple sclerosis	11	Patients	NR	Semi-structured interview	Offline	Phenomenological analysis
Smith et al. 2010	United States	NR	General knowledge about warfarin therapy among the atrial fibrillation population	100	Patients	NR	Questionnaire	Offline	NR
Tsele-Tebakang, Morris-Eyton, and Pretorius 2022	South Africa	2018–2019	The perceptions and revelations of primary healthcare nurses regarding the use of herbal medicine; whether nurses communicate to their patients about herbal medicine and address the anticipated HDL.	8	Nurses	NR	Semi-structured interview	Offline	Thematic framework analysis

(Continues)

TABLE 1 | (Continued)

ID	Country/region of research conduct	Research duration	Research focus	Sample size	Role of participants	Participants' race or ethnicity	Data collection method	Form of data collection	Qualitative data analysis method
Tsele-Tebakang, Morris-Eyton, and Pretorius 2023	South Africa	NR	patients' perception and use of herbal medicine and their knowledge of HDI.	30	Patients	NR	Focus groups	Offline	Thematic content analysis
Vickers, Jolly, and Greenfield 2006	United Kingdom	NR	Women's perspectives on the safety of herbal remedies, HDI, and communication with healthcare professionals regarding herbal medicines.	18	Patients	White British	Semi-structured interview	Online	Thematic framework analysis
Watt et al. 2012	Canada	2007.12–2009.12	Chinese immigrant parents' perception about the use of CAM in their child with cancer	25	Parents of children with cancer	Chinese and South Asian Canadian	Semi-structured interview	Offline	Grounded theory
Williamson and Maguire 2008	United Kingdom	NR	Oncology patients and staff on their attitudes to CAMs	44 5 4	Patients Nurses Pharmacists	NR	Interview	Offline	NR

Abbreviations: CAM, complementary and alternative medicine; HDI, herb-drug interactions; KAP, knowledge, attitudes, and practices; MRPs, medicine-related problems; NR, not reported.

TABLE 2 | CASP appraisal results for the included studies.

ID	Was there a clear statement of the aims of the research?	Is a qualitative methodology appropriate?	Was the research design appropriate to address the aims of the research?	Was the recruitment strategy appropriate to the aims of the research?	Was the data collected in a way that addressed the research issue?	Has the relationship between researcher and participants been adequately considered?	Have ethical issues been taken into consideration?	Was the data analysis sufficiently rigorous?	Is there a clear statement of findings?	How valuable is the research?
Alhomoud 2014	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Christensen et al. 2017	Yes	Yes	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes
Dharmarajan et al. 2006	Yes	Yes	Yes	Yes	Yes	Can't tell	Can't tell	Can't tell	Yes	Yes
Gokcekus et al. 2012	Yes	Yes	Yes	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes
Little et al. 2018	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes
Makkaoui et al. 2020	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Meshesha et al. 2020	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Moen et al. 2009	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Muñoz et al. 2013	Yes	Yes	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes
O'Callaghan and Quine 2007	Yes	Yes	Yes	Yes	Yes	Can't tell	Can't tell	Yes	Yes	Yes
Odegard et al. 2022	Yes	Yes	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes
Skovgaard, Pedersen, and Verhoef 2014	Yes	Yes	Yes	Yes	Yes	No	Can't tell	Yes	Yes	Yes
Smith et al. 2010	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Can't tell	Yes	Yes

(Continues)

TABLE 2 | (Continued)

ID	Was there a clear statement of the aims of the research?	Is a qualitative methodology appropriate?	Was the research design appropriate to address the aims of the research?	Was the recruitment strategy appropriate to the aims of the research?	Was the data collected in a way that addressed the research issue?	Has the relationship between researcher and participants been adequately considered?	Have ethical issues been taken into consideration?	Was the data analysis sufficiently rigorous?	Is there a clear statement of findings?	How valuable is the research?
Tsele-Tebakang, Morris-Eyton, and Pretorius 2022	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Tsele-Tebakang, Morris-Eyton, and Pretorius 2023	Yes	Yes	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes
Vickers, Jolly, and Greenfield 2006	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes
Watt et al. 2012	Yes	Yes	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes
Williamson and Maguire 2008	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Can't tell	Yes	Yes

from various sources, such as general practitioners, CAM practitioners, pharmacists, leaflets, herbal medicine sales agent, internet, and nurses (Alhomoud 2014), (Christensen et al. 2017), (O'Callaghan and Quine 2007), (Skovgaard, Pedersen, and Verhoef 2014), (Tsele-Tebakang, Morris-Eyton, and Pretorius 2023). Many healthcare professionals consulted pharmacists for their professional knowledge (Little et al. 2018). Pharmacists mostly relied on fundamental concepts acquired during their education, supplemented by hands-on practice and aided by software and websites, to gather insights on HDIs (Makkaoui et al. 2020). However, they encountered unsatisfactory supplementary resources with conflicting information, insufficient details on HDIs, and poor user-friendliness (Makkaoui et al. 2020). These challenges often led to time-consuming processes when determining HDI risks.

When it came to healthcare professionals' level of knowledge of HDIs, there was a noticeable disparity. While they did acknowledge the term of "HDI," they often faced challenges when asked to providing specific examples (Williamson and Maguire 2008), (Tsele-Tebakang, Morris-Eyton, and Pretorius 2022). Pharmacists admitted that their understanding of HDIs may be incomplete and outdated, leaving gaps in their ability to effectively address and prevent such interactions (Makkaoui et al. 2020). This lack of concrete knowledge not only signified an inadequate awareness of potential HDIs among healthcare professionals but also highlighted its insufficiency in guiding their clinical decision-making process (Meshesha et al. 2020).

"If I (prescriber) asks the patient whether he/she has been using herbal medicine and found that he/she was using any herb, I wouldn't take any decision towards using herb because I don't have any knowledge about a specific herb and the conventional anti-diabetic drug interactions." (Makkaoui et al. 2020)

Regarding patients, it was widely acknowledged that the simultaneous use of herbs and western medicine carried the risk of potential adverse HDIs (O'Callaghan and Quine 2007). As a precautionary measure, patients often adopted a strategy of taking herbs and western medicine at separate intervals (O'Callaghan and Quine 2007). They also disapprove of the practice of using one medication to treat adverse reactions caused by another medication (Moen et al. 2009). However, it was important to note that patients faced difficulties in fully comprehending the concept of HDI (Moen et al. 2009). Many patients held the view that HDI had the potential to nullify the effects of another medicine (Christensen et al. 2017). Nevertheless, they often held the belief that certain scenarios would not result in adverse HDIs. These scenarios included: (1) the use of herbs with mild medicinal properties; (2) when the diseases being treated were not severe; and (3) when herbs and western medicine were employed to target different diseases, respectively (Vickers, Jolly, and Greenfield 2006).

"No I think ginseng is quite mild so it is unlikely to react with medication. If I was taking herbal then I wouldn't

take prescribed for the same problem. It also depends on what is wrong with you. I don't think that things I take for say the immune system or detox or to boost your mood would react with something like antibiotics" (Vickers, Jolly, and Greenfield 2006)

In terms of role responsibilities, patients and community pharmacists thought that CAM physicians, pharmacists, and general practitioners were all deemed capable or responsible for assessing potential HDIs in patients' medication and providing appropriate medication guidance and counseling (Alhomoud 2014), (Gokcekus et al. 2012), (Makkaoui et al. 2020). Among these healthcare professionals, pharmacists were considered by patients to have a greater responsibility for professionally assessing medication from a knowledgeable standpoint (Makkaoui et al. 2020). Patients also expressed their desire for pharmacists to provide additional medication information that doctors may not always offer (Alhomoud 2014). However, it was reported that some community pharmacists had not consistently made it a routine to detect drug interactions (Makkaoui et al. 2020). Moreover, Lebanon pharmacists have disclosed that in certain countries or regions like Lebanon, the role of pharmacists in managing HDIs was marginalized, with patients tending to place more trust in doctors than in pharmacists.

"A few participants have attributed a higher role for the physicians to detect drug interactions, claiming that in the Lebanese culture, the role of pharmacists is marginalized and less trusted by patients than that of doctors." (Makkaoui et al. 2020)

3.3.2 | Attitudes

In terms of their attitude toward HDIs, two distinct themes emerged: affective tendency and behavioral tendency. The affective tendency refers to the concerns or personal evaluations of HDI from an emotional or subjective perspective, which can be further divided into two opposing categories. Firstly, some patients expressed concern that adverse interactions between herbs and conventional medications might have detrimental effects on their health (Christensen et al. 2017), (Odegard et al. 2022). They worried that these interactions could potentially compromise the effectiveness of the prescribed medication, resulting in a waste of money (Christensen et al. 2017).

"I don't want to get sicker than I already am. A lot can interact and kill you, alternative and otherwise." (Christensen et al. 2017)

On the other hand, some patients held a perception that herbs were beneficial and natural, which led them to be less concerned about potential adverse HDIs (Skovgaard, Pedersen, and Verhoef 2014). This belief might stem from a preference for natural remedies and a belief in the healing powers of herbs. Consequently, they may overlook the risks associated with HDI.

“Yeah, well, I suppose they could [interact]. But I sort of feel that it’s nature. Uhm, so it’s not something I am afraid of.” (Skovgaard, Pedersen, and Verhoef 2014)

Patients exhibited two main behavioral inclinations when they were faced with the knowledge that the herbs they were using may interact with their western medicine. Firstly, they were likely to consult with their CAM practitioner or general practitioner for further guidance and advice (Williamson and Maguire 2008). This showed their willingness to seek professional input in order to ensure their safety and avoid potential adverse HDIs. Secondly, some patients chose to discontinue the use of herbs altogether when they were informed of potential HDIs (Williamson and Maguire 2008). Similarly, some individuals opted not to take their herbs and prescribed medications for the same condition (Vickers, Jolly, and Greenfield 2006).

“When asked what they would do if they were told that their CAMs interacted with their conventional treatment, 10 patients said they would stop taking it, one said they would consult their GP and one said they would consult their CAM practitioner.” (Williamson and Maguire 2008)

3.3.3 | Practices

Within the practice theme, three analytical themes emerged: medication regimen, medication assessment, and medication counseling/guidance. Patients’ approaches to combining herbs and western medicine were found to align with their personal understanding. For instance, some patients would discontinue western medicine use while on herbs, while others would time their intake of herbs and western medicine at intervals to maximize therapeutic benefits and minimize adverse interactions (O’Callaghan and Quine 2007). However, there were also cases where patients would concurrently take both herbs and Western medicine (Vickers, Jolly, and Greenfield 2006).

“I take Western and Eastern medicine separately, about one hour apart, even with different kinds of Western medicine that the doctor prescribed.” (O’Callaghan and Quine 2007)

In terms of medication assessment, pharmacists played a crucial role in evaluating the presence of HDIs in medications. However, it was found in Lebanon that not all pharmacists consistently check for HDIs in their practice, citing various reasons, such as time limitations, patients’ tendency to rely on doctors, as well as the claim that it is simply not a common practice in Lebanon or that they are not adequately trained for that (Makkaoui et al. 2020). Although some healthcare professionals inquired patients about the use of herbs to assess HDI risks, some nurses and pharmacists typically assessed for HDIs only when there was a significant concern or if the interaction was deemed highly dangerous (Makkaoui et al. 2020). Furthermore, pharmacists tended to report only the most commonly known HDIs they had learned through their practice (Makkaoui et al. 2020).

“As for the practices, the majority of the interviewees reported that they do not always check for drug interactions ... Excuses included time limitations in their interactions with patients, the tendency of the patient to rely on doctors, as well as the claim that it is simply not a common practice in Lebanon, or that they are not adequately trained for that.” (Makkaoui et al. 2020)

With regards to medication counseling, physicians and pharmacists did not proactively provide information about HDIs to patients. Some physicians cited a lack of knowledge in this area, while others directly advised patients to stop using herbs when they learned that patients were using herbs together with western medicine (Meshesha et al. 2020), (Tsele-Tebakang, Morris-Eyton, and Pretorius 2022). However, it was also noted that healthcare professionals may not pay attention to the patient’s history of herb use (Meshesha et al. 2020). Some patients informed healthcare professionals about their herbal medication use in order to avoid adverse HDIs, while others did not inform physicians because they felt the physicians were not interested or held a negative attitude towards herbs (Christensen et al. 2017), (O’Callaghan and Quine 2007), (Vickers, Jolly, and Greenfield 2006). Some patients consulted pharmacists, while others did not discuss medication-related problems (MRPs) with pharmacists because they believed that pharmacists were only responsible for providing medications (Alhomoud 2014).

“Yes, he [pharmacist] always gives good advice about my medicines and my wife’s medicines like indications, contraindications, reactions with other tabs... This kind of specific information that the doctor would not give thoroughly... Like my wife, her doctor, the one we like to see most, is putting her on lots of changes and those changes are happening very quickly... Like they put her on new tabs and these tabs started giving her wheezing effect so I had to run to the GP to get some Ventolin and I had to run to here to have the Ventolin dispensed... Those contraindications between different tabs were not explained thoroughly by the GP... Since then I started asking the pharmacist about every changes me and my wife has.” (Alhomoud 2014)

3.3.4 | Experiences

Within the experience theme, two second-level themes were identified: healthcare and consultation experience, and medication experience. Based on patients’ healthcare experiences and consultations, it was observed that healthcare professionals, especially physicians, generally inquired about patients’ use of CAM to investigate potential risks associated with HDIs (Christensen et al. 2017). However, they often fell short in providing specific and helpful information regarding HDIs, preferring instead to focus on simply alerting patients to these risks (Skovgaard, Pedersen, and Verhoef 2014), (Tsele-Tebakang, Morris-Eyton, and Pretorius 2023). Moreover, there appeared to be a lack of interest on the part of physicians when patients attempted to

discuss their use of herbs, showing little concern for potential adverse HDIs (Skovgaard, Pedersen, and Verhoef 2014). Nurses have provided feedback that patients did not disclose their use of herbal medicine when prescribed conventional medication (Tsele-Tebakang, Morris-Eyton, and Pretorius 2022).

"I've told them about the different things I take, so they know about it, but they don't really care that much. 'I see, I see', is all they say. My former physician thought it was very fascinating and very interesting, but then, unfortunately, he left. And these new ones, they're not as.... 'I see, I see', they say. I don't think they believe in it at all." (Skovgaard, Pedersen, and Verhoef 2014)

Pharmacists, on the other hand, sometimes primarily directed patients to consult physicians when it came to managing MRPs, including potential HDIs (Alhomoud 2014). Both physicians and pharmacists tended to offer limited information regarding drug interactions unless explicitly requested by the patient. (Alhomoud 2014; Gokcekus et al. 2012) But some patients trust in CAM practitioners' knowledge and expertise in avoiding negative HDIs (Skovgaard, Pedersen, and Verhoef 2014).

"And he [the CAM practitioner] knows full well (...) he sees many, many sclerosis patients at his clinic, so he has a lot of experience with it, and he would never give me something he thinks might make me sick, I just don't think he would. So I fully trust him, and it's not the case that I take all kinds of different strange things. I don't just buy some herbal medicine and eat it." (Skovgaard, Pedersen, and Verhoef 2014)

3.3.5 | Expectations and Information Needs

In the theme of expectations and information needs, four secondary themes were identified: knowledge information, medication alert, patient–physician communication, and herbal supplements labeling. Regarding the combination use of herbs and western medicine, patients wanted to learn or hoped that healthcare professionals could provide information on HDIs, such as whether the drug combination could enhance efficacy, whether herbs affected the efficacy of regular dosage of the given medication, whether combined medication was appropriate for individual cases (such as hypertension patients), and how long it was necessary to space out the intake of western medicine and herbal medicines (Christensen et al. 2017), (O'Callaghan and Quine 2007). Some patients hoped to receive HDI alert information, which could include directly from physicians, through a kiosk during doctor visits, via a smartphone application, personal health record, at the pharmacy, through print or email, and so forth (Christensen et al. 2017). Methods of providing information might include written, verbal, telephone, face-to-face, website, TV in waiting areas, email, or at home (Christensen et al. 2017). It is worth noting that some patients indicated that they wanted to receive HDI medication alert from individuals/sources, other than physicians and pharmacists, as a "fail-safe" mechanism to prevent omission by physicians or pharmacists. (Christensen et al. 2017) In addition, patients wanted to

know the safety outcomes (such as sequelae), long-term consequences, and severity of adverse drug interactions (Christensen et al. 2017).

"I don't want to have a stroke. I would be really interested. Need to know all possible after-effects. [...] I am chemically sensitive." (Christensen et al. 2017)

In terms of communication between physicians and patients, patients wished to be involved in making decisions about their medications (Christensen et al. 2017). They wanted to understand the potential HDIs that could occur when different medications were combined and how these interactions might affect their own physical conditions. Additionally, some patients expressed a desire to have information about potential HDIs included in the labels or instructions for herbal preparations. They also wanted to know what actions to take if adverse HDIs happened (Vickers, Jolly, and Greenfield 2006).

"Doctors should not act like God or something. They should listen to patients and take their advice on what works for their bodies." (Christensen et al. 2017)

4 | Discussion

4.1 | Summary of Results

The synthesis of data from 18 included studies (Alhomoud 2014), (Christensen et al. 2017), (Dharmarajan et al. 2006), (Gokcekus et al. 2012), (Little et al. 2018), (Makkaoui et al. 2020), (Meshesha et al. 2020), (Moen et al. 2009), (Muñoz et al. 2013), (O'Callaghan and Quine 2007), (Skovgaard, Pedersen, and Verhoef 2014), (Smith et al. 2010), (Vickers, Jolly, and Greenfield 2006), (Watt et al. 2012), (Williamson and Maguire 2008), (Odegard et al. 2022), (Tsele-Tebakang, Morris-Eyton, and Pretorius 2022), (Tsele-Tebakang, Morris-Eyton, and Pretorius 2023) revealed several key insights into healthcare professionals', pharmacists', and patients' perspectives, attitudes, practices, experiences, and expectations regarding HDIs. Healthcare professionals, including pharmacists, demonstrated a varied understanding of HDIs, with some acknowledging the term but facing challenges in providing specific examples (Williamson and Maguire 2008), (Tsele-Tebakang, Morris-Eyton, and Pretorius 2022). Pharmacists, in particular, relied on their basic knowledge supplemented by practical experience, yet encountered difficulties due to conflicting information sources and inadequate training (Makkaoui et al. 2020). Patients exhibited a cautious approach toward HDIs, often adopting preventive measures such as separating the intake of herbs and western medicine (O'Callaghan and Quine 2007). Despite their concerns, patients displayed mixed attitudes toward the potential risks of HDIs, reflecting both apprehension and trust in the natural benefits of herbal remedies (Christensen et al. 2017), (Skovgaard, Pedersen, and Verhoef 2014), (Odegard et al. 2022). However, patients encountered obstacles in fully grasping the concept of HDIs, which underscores the importance of comprehensive education and communication from healthcare professionals (Alhomoud 2014), (Gokcekus et al. 2012), (Makkaoui et al. 2020).

CAM physicians, pharmacists, and general practitioners were considered by patients to possess the ability or responsibility to assess potential HDIs in patients' medication (Makkaoui et al. 2020). However, physicians and pharmacists did not actively provide information about HDIs to patients, and in some cases, physicians directly advised patients to discontinue using herbs (Meshesha et al. 2020), (Tsele-Tebakang, Morris-Eyton, and Pretorius 2022). Healthcare professionals, including pharmacists, typically checked interaction information in their clinical practice, but they usually only assessed HDIs when they were deemed to have significant clinical importance or caused serious adverse effects (Makkaoui et al. 2020). Patients expressed a desire for more proactive involvement in medication decisions and comprehensive information on HDIs, emphasizing the importance of patient-centered care in addressing HDIs effectively (Christensen et al. 2017), (Vickers, Jolly, and Greenfield 2006).

4.2 | Advantages and Limitations of the Study

The main purpose of this qualitative SR was to systematically evaluate the qualitative research results on HDIs from different countries/regions, cultural backgrounds, using different methodologies and synthesis of themes, in order to understand the perspectives, experiences and clinical practices of healthcare professionals, pharmacists, and patients regarding HDIs. It is hoped that this information can provide an understanding of personal perceptions and challenges when using HDIs in clinical practice. The quality of individual qualitative studies was assessed using CASP, and the quality of the research was high, with a relatively large population of studies included. The evidence synthesis results are based on high-quality qualitative studies or mixed-methods research. However, this study still has limitations. The CASP results indicated that the studies using convenience sampling or purposive sampling may have selection bias, which may limit the generalizability and applicability of the study results (Long, French, and Brooks 2020), (Wilson and Anagnostopoulos 2021). Qualitative research relies on a deep understanding and interpretation of data. If the methodology is not clear, it may weaken the credibility and reliability of the research (Roulston 2010). Populations in different countries were included and some evidence synthesis results were based on individual studies. Different countries have different systems and cultural background, and this may lead to very different practices and perspectives. No studies had been conducted in China, and some studies limited the study subjects by race. The influence of cultural and regional factors in China, with its unique medical and cultural background, has different herbal usage habits, healthcare systems, and patient expectations compared to other regions (Ye et al. 2022) (Williamson et al. 2013). Neglecting research in China could limit global understanding of these factors regarding HDIs. In this specific situation, the synthesized cognitive, experiential, and behavioral practices may not be applicable or generalizable to other countries especially given this review was conducted on qualitative studies.

4.3 | Insights for Clinical and Future Research

Firstly, there may be insufficient attention paid to HDIs in clinical practice due to a lack of knowledge. Previous research has

indicated that regarding traditional and complementary healthcare approaches (TCAs) in UK, parents tended to be more practical, assessing what falls under TCA and how effective they perceive it to be. In contrast, practitioners tended to focus on theoretical aspects, especially endorsing TCAs with plausible mechanisms of action and supporting research evidence (LorencA and Robinson 2010). Thus, it is crucial for practitioners to understand the breadth and depth of TCAs utilized and the motivations behind their use. Engaging in discussions with families about whether these approaches can be safely and acceptably integrated with current medical treatments is essential (LorencA and Robinson 2010), (Lorenc, Blair, and Robinson 2014). Another UK study (Robinson and Lorenc 2010) found results consistent with ours, revealing that pharmacists wished to increase their knowledge as information on herbal and nutritional products (HNPs) was limited, and the need to maintain professionalism at all times was recognized. Pharmacists appeared to understand and empathize with customer demand for HNPs and were uniquely positioned within the National Health System to provide product advice and support in UK. However, to maintain professionalism, pharmacists might have required further information on HNPs and continuing professional training, especially the HDIs with prescribed and over-the-counter drugs. To address this, education for healthcare professionals is needed to incorporate comprehensive training (Dores et al. 2023) on HDIs, covering basic knowledge, assessment methods, and counselling practices. Continuing education programs are also advocated to be implemented to update healthcare professionals on the latest research and developments in the field of HDIs. To promote the communication between patients and healthcare professionals, including pharmacists, healthcare professionals ought to adopt proactive approaches in assessing and managing HDIs, ensuring that patients receive accurate information and appropriate guidance.

Secondly, there is a pressing need for government bodies and policymakers to prioritize the regulation and management of HDIs. A study conducted in US (Ronis, Pedersen, and Watt 2018) revealed that unlike foods or drugs, herbal supplements do not require preapproval or registration by the US Food and Drug Administration (FDA) before production or sales. The FDA is restricted to post-marketing adverse report monitoring under the Dietary Supplement Health and Education Act of 1994. Policies might be considered to be formulated to mandate the inclusion of HDI education and training in healthcare curricula, ensuring that healthcare professionals are adequately equipped to address HDIs in clinical practice. Additionally, regulations could be established to promote collaboration between conventional and complementary medicine sectors for comprehensive patient care.

Thirdly, education campaigns targeting consumers could also be developed to increase awareness of HDIs and empower patients to make informed decisions about their healthcare. Consistent with our research findings, patients often failed to disclose their supplement usage to their physicians, resulting in a significant risk of adverse drug-herbal supplement interactions (Ronis, Pedersen, and Watt 2018). Consumers should be provided with accessible and reliable information on the potential risks and benefits of combining herbs and conventional medications. Moreover, collaboration and communication are crucial for investigating the causality of HDIs and assessing

the clinical benefits and risks in patient care. It is essential for all team members, including the patient, to engage in the discussion (Souza-Peres et al. 2023). Thus, strategies could also be implemented to improve patient-provider communication, facilitating open discussions about herbal use and potential HDIs during clinical consultations.

Lastly, future research efforts may consider focus on filling knowledge gaps related to HDIs, investigating the perspective, attitude, and practices on of CAM practitioners, particularly in regions with unique cultural and healthcare contexts like China. Qualitative studies can provide valuable insights into patients' perspectives, attitudes, and practices regarding HDIs, while quantitative studies are needed to assess the prevalence and clinical significance of HDIs. Collaborative research initiatives involving multidisciplinary teams can drive innovation in HDI assessment methods, pharmacovigilance systems, and clinical decision support tools, ultimately improving patient outcomes and healthcare quality.

5 | Conclusion

Our study results indicate that healthcare professionals and pharmacists have a limited understanding of HDIs, leading to a lack of attention to HDIs in clinical practice. Patients primarily rely on physicians and pharmacists for information on medications, and they are particularly concerned about the potential occurrence and severity of adverse HDIs, the impact on drug effectiveness, and the appropriate timing between doses when combining herbs with western medicine. Patients hope to receive clear HDI alerts in this regard. Furthermore, the study findings suggest that healthcare professionals need to improve their focus on and knowledge of HDIs and enhance communication with patients. Attention is needed from government, policymakers, healthcare professionals, and education system. It is also recommended to conduct further investigations and research on the knowledge and practices of CAM practitioners in China. This would serve as a warning for existing issues in clinical practice and provide guidance for the safe use of medications.

Author Contributions

Chen Shen: conceptualization, data curation, formal analysis, investigation, methodology, project administration, resources, software, supervision, validation, visualization, writing – original draft, writing – review and editing. **Zhi-Ying Ren:** investigation, validation, writing – review and editing. **Hui-Di Lan:** investigation, resources, validation, writing – review and editing. **Ling-Yao Kong:** investigation, resources, validation. **Ming Yang:** conceptualization, methodology, writing – review and editing. **You-Zhu Su:** writing – original draft, writing – review and editing. **Xiao-Lei Yue:** investigation, validation. **Zu-Lin Wan:** investigation, validation. **Li-Xue Xiao:** investigation, validation. **Pi-Pi Chen:** investigation, validation. **Xun Li:** methodology, writing – review and editing. **Xian Zhou:** supervision, writing – review and editing. **Nicola Robinson:** supervision, writing – review and editing. **Jian-Ping Liu:** conceptualization, funding acquisition, methodology, project administration, supervision, writing – review and editing.

Ethics Statement

The authors have nothing to report.

Consent

The authors have nothing to report.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data generated during and/or synthesized during the current study are available from the corresponding author upon reasonable request.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.