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Conceptual graph-based knowledge representation for supporting reasoning in African traditional medicine

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ABSTRACT

Although African patients use both conventional or modern and traditional healthcare simultaneously, it has been proven that 80% of people rely on African traditional medicine (ATM). ATM includes medical activities stemming from practices, customs and traditions which were integral to the distinctive African cultures. It is based mainly on the oral transfer of knowledge, with the risk of losing critical knowledge. Moreover, practices differ according to the regions and the availability of medicinal plants. Therefore, it is necessary to compile tacit, disseminated and complex knowledge from various Tradi-Practitioners (TP) in order to determine interesting patterns for treating a given disease. Knowledge engineering methods for traditional medicine are useful to model suitably complex information needs, formalize knowledge of domain experts and highlight the effective practices for their integration to conventional medicine. The work described in this paper presents an approach which addresses two issues. First it aims at proposing a formal representation model of ATM knowledge and practices to facilitate their sharing and reusing. Then, it aims at providing a visual reasoning mechanism for selecting best available procedures and medicinal plants to treat diseases. The approach is based on the use of the Delphi method for capturing knowledge from various experts which necessitate reaching a consensus. Conceptual graph formalism is used to model ATM knowledge with visual reasoning capabilities and processes. The nested conceptual graphs are used to visually express the semantic meaning of Computational Tree Logic (CTL) constructs that are useful for formal specification of temporal properties of ATM domain knowledge. Our approach presents the advantage of mitigating knowledge loss with conceptual development assistance to improve the quality of ATM care (medical diagnosis and therapeutics), but also patient safety (drug monitoring).

1. Introduction

In many regions in the world (including Africa, Asia and America) traditional medicine is a socio-cultural reality which has provided a scientific contribution to modern medicine. Given the deficiency of medical doctors in developing countries, traditional health practitioners (THPs) contribute tremendously to healthcare coverage. In some cases, traditional medical practitioners use medicinal plants that have not been actively used in modern medicines (Cragg and Newmann, 2005).

Nowadays, there is a renewed interest in the western world for plants used in traditional medicine that is regularly mixed with orthodox medicines in developing countries. Traditional medicine is "the total sum of knowledge, skills and practices based on the theories, beliefs and experiences indigenous to different cultures, whether explicable or not, used in the maintenance of health and in the prevention, diagnosis, improvement or treatment of physical and mental illness." (WHO, 2004). Traditional medicines (TM) have incorporated a lot of empirical knowledge combining physical, mental, emotional or social well-being and reflecting the cumulative body of local knowledge that is passed onto generations by oral transmission through *traditional health practitioners (THPs) and knowledge holders* (Sackey and Kasilo, 2010). African traditional medicine (ATM) has a holistic view on healthcare involving extensive use of physiotherapy and herbalism sometimes combined with some aspects of African spirituality (Onwuanibe, 1979). A disease is often seen in African TM as the failure of complex physical, social and spiritual relationships. Therefore, a diagnosis starts with an examination of both human and supernatural interactions. For instance, when the ailment is mystical, ritual diagnosis is a fundamental part of the traditional

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healing process for re-establishing social and emotional equilibrium (Tella, 1979). Particularly, the philosophical clinical care embedded in African traditions, culture and beliefs have contributed to making TM practices acceptable and hence highly demanded by the population (Mhame et al., 2010), estimated by the WHO about 80% of people. Indeed, compared to modern practitioners, African Traditional Practitioners (ATP) interact very differently with their patients, using a more patient-centered communication style, to reach common ground with sick persons (Labhardt et al., 2010). Considering sociological and economical factors, TM is a vital health-care resource in developing countries and it contributes positively to the primary healthcare delivery of the local populations, as usually TM appears to be more affordable and less expensive than pharmaceutical drugs for the majority of patients living in Africa. Generally, the experiences have been field-tested for centuries and the relationship of the local people with their ecological systems is codified through language and culture (Martha, 1992). According to the holistic perspective of ATM, the external and internal environment of a patient is considered in the understanding, the prevention, and treatment of diseases. Contrary to the principle of conventional medicine, ATM uses commonly natural products of which the advantage over synthetic compounds rests on their intrinsic potential to provide mild healing effects and induce fewer side effects (Lukman et al., 2007). Meanwhile, both in ATM and conventional medicine, the foundation of disease treatment relies on the correspondences between the clinically active compounds and their biological targets at the molecular level.

The various formats of traditional knowledge are mostly tacit and therefore largely shared in unstructured format. Furthermore, with the lack of scientific evidence on the effectiveness of TM, there are some differences between the healing properties firmly rooted in collective imagination and the therapeutic knowledge actually associated to medicinal plants (Kale, 1995). Many plants have been postulated to have similar activities to pharmaceutical drugs. However, they have not been extensively assessed scientifically in terms of their biological activities (WHO, 2002). Many people believe that because medicinal plants are natural, they are safe with dangers (or not likely to damage something) of an unknown pharmacopoeia. However, TM and its practice, can cause adverse reactions and be harmful if the product or treatment is poor, or if applied improperly or in conjunction with other drugs. The factors of adverse events are numerous. They include misidentification, adulteration, wrong labeling, contamination with toxic or hazardous substances, over dosage, misuse of herbal medicines by either healthcare providers or consumers and use of herbal medicines concomitantly with other medicines (Kasilo and Trapsida, 2010). It is important that patients become more aware of these risks and proceed with caution. Moreover, traditional practitioners need better training and active collaboration and communication between them has to be encouraged.

There is also a need to formalize the most commonly used knowledge for TM, in order to enhance and broaden the long historical use of these medicines. Emphasis should be placed on the need for formalization of traditional health knowledge, which can contribute to discovery and development of new traditional and orthodox medicines (Sambo, 2010). Following the example of biomedicine, the knowledge might at least be well documented with grammatical statements, mathematical expressions, and specification and perhaps consolidated with scientific considerations and substantiation. The documentation and verification of this knowledge can be made towards a formal framework for the search of effective herbal medicines and an education scheme will be phased in gradually for the effective contribution of traditional medicines to mainstream healthcare (Puckree et al., 2002). Only a few countries in Africa (e.g. Ghana and Nigeria) have developed national herbal pharmacopoeias to document medicinal plants that have been found to be effective and to further ensure their safety, efficacy and quality. After their publication, these pharmacopoeias have helped substantiate the alternative medical uses of many African medicinal plants; information on well-controlled clinical evaluations is almost unavailable (Kasilo et al., 2010). For instance, some African plants (e.g. *Asparagus africanus* (Liliaceae), *Crinum glaucum* (Amaryllidaceae) and *Aframomum melegueta* (Zingiberaceae)) are reported to be used in the context of age-related cognitive disorders (e.g. Alzheimer's disease, dementia and memory loss (Adams et al., 2007). In this case, inhibition of the enzymes acetylcholinesterase or monoamine oxidase B seems to be the mechanism of action (Stafford et al., 2008).

Establishing traditional medical resources and knowledge related databases would contribute to document prescriptions used in TM to prevent mismanagement (e.g. poor modes of prescription). This is a prerequisite for a development of a formal methodological framework aiming at the support of traditional medical practitioners and patients in selecting and applying the most appropriate herbal medicines with means to detect flaws in the medical practices and to perform corrective actions. Such a framework would promote the acquisition of knowledge and skills by facilitating the exchange of experiences between traditional medicine practitioners (TMPs) or collaboration between Conventional Medicine Practitioners (CHPs) and TMPs in areas such as referral of patients. There is therefore a need to look for methods of formalizing endogenous knowledge in traditional medicine. This may provide baseline knowledge on the African medicinal plants, feasible pharmaceutical uses and threats to sustainable usage (Ndenecho, 2009). The research work reported in this paper falls within this vision. To do so, our proposal is based on the use of conceptual graphs for temporal properties specification of ATM knowledge in which domain-specific units of knowledge are described with a visual modeling approach instead of expressing by logical formulas. Conceptual graphs benefit from a solid logic foundation and their mode of formal reasoning can rely on logical operators or on graph–theoretical operations.

The rest of the paper is structured as follows. Section 2 exposes the state of the art concerning knowledge acquisition and formalization for ATM and conceptual graph formalism. We outline preliminaries and background regarding the way research scientists and medical doctors capture practices of African Traditional Practitioners. In addition, a motivated case study from the West African sub-region (Guinea) is presented in order to give an actual illustration of the reality in ATM. We detail in Section 3 our approach of formal representation of a set of concepts of ATM domain knowledge and their relationships. Section 4 presents the framework used to implement the conceptual graphs for ATM knowledge formalization and in Section 5 our approach is showcased through an illustrative example treating public health issues in Cameroon. We demonstrate that the proposed formalization approach is capable of tracking and evaluating situations with medicinal plants that may affect Cameroonian health. Finally, Section 6 concludes and discusses future challenges.

2. State of the art

2.1. Background on capturing TMPs knowledge

In order to facilitate the understanding of the approach that we propose in this paper, we outline in this section the process followed for identifying and selecting the interesting plants for treating a given disease and their mechanism of use in a therapeutic prescription (see Fig. 1).

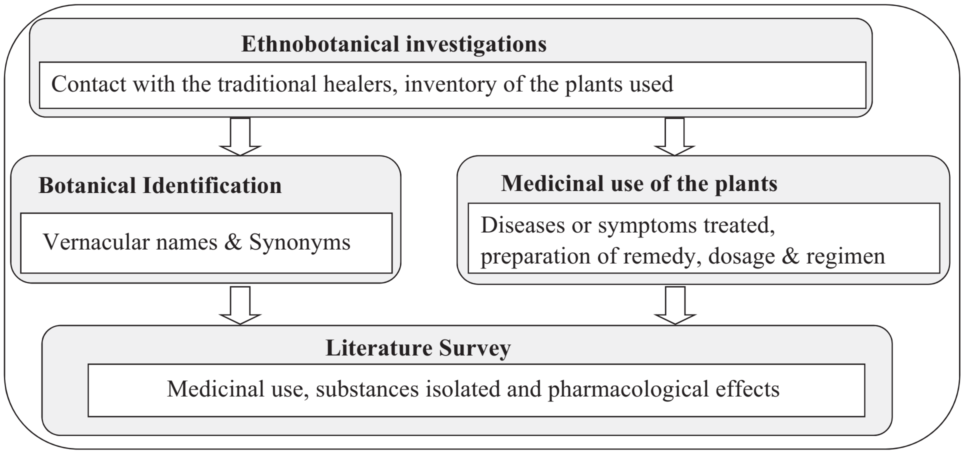

Fig. 1. Process for the study of African traditional medicinal plants.

The resources about plants used by the traditional healers comprises botanical identification of the plants (synonyms and vernacular name), the part of the plant used (e.g. roots, leaves, stem and stem bark, fruits and seeds) and available prescriptions of the medicinal use of the plant including diseases treated, preparation of remedies (e.g. crushed, powdered or boiled) and dosage. In addition, a literature review should be conducted, comprising previously reported medicinal uses of the plants, and substances isolated as well as observed pharmacological effects (Samuelsson et al. 1991).

The main sources used by the research scientist and medical doctor interested in ATM, named hereby the investigator, are the traditional medicinal practitioners (TMPs), the patients and the scientific literature.

The first step is to select the disease to focus on. A survey is conducted in order to inventory the most cited plants used by TMPs and the inhabitants to treat the concerned disease. Moreover, the plant part used for the treatment is also identified. Thus, for a given disease, the essential part for a given plant can be the bark, its leaves or roots, etc. The TMPs that actively use the plants and who usually have a good reputation in terms of efficiency among people are identified by the investigator. According to the disease, a prevalence study is conducted. This study measures the importance of the disease in that area. The more frequent a disease is the higher the chance to get patients to observe during the study.

The second step is to perform a set of ethno-botanical and bibliographic surveys. As the TMPs use the local name of medicinal plants also known as vernacular names, the investigator needs to identify its scientific name. Local lexicons are developed in most countries to facilitate this process. This name is used to lookup the scientific literature, including the MedLine database through the PubMed portal (Pubmed, 2011) and major medical journals. If any scientific publication reports a significant study about the plant, then an ethno-therapeutical investigation in real conditions with the selected healer is conducted by the investigator. To do so, and in order to cope with the common dosage issue (Bayor et al., 2010), the investigator usually asks the healer to prepare a fixed number of treatments. The experts from Cameroon and Guinea that we have interviewed use roughly the same process. In TM, the notion of dosage is often vague. Indeed, the palm of the hand is commonly used as reference; knowing that a child differs from that of an adult, and so on. In this perspective, from the fixed number of doses prepared by the healer, the investigator establishes a baseline average for the dosage. Thus, he/she measures the biological parameters of the patient being observed (before, during and after) the medication. If the step is successful, a phytochemical study is conducted to establish the genetic fingerprint of the plant and produce the pharmaceutical formulation of the future drug. If the step is unsuccessful because of the important side effects for instance, the investigator usually decides to stop the process.

After the identification of a suitable plant for a given disease, a further step is required. Indeed, the approval for commercialization of recipes from the medicinal plants requires evaluation of their scientific evidence. This includes initiatives supporting the toxicity tests followed by additional biological galenic tests and clinical trials. In fact, limited plant species that provide medicinal herbs have been scientifically evaluated for their possible medical applications; although the data ensuing from preclinical trials are encouraging, there have been insufficient comparative clinical studies. So, there is a fundamental requirement to create facilities for a sound, scientific understanding and specialized training based on applied chemical, biological and pharmaceutical principles (Adewunmi and Ojewole, 2005).

According to the process described above, there is a need for a formal knowledge acquisition method in order to capture and formalize the different phases. The Delphi method (Milholland et al., 1973) seemed appropriate in capturing collective knowledge. Indeed, Delphi is well suited for capturing and capitalizing knowledge from multiple experts and it supports the process of development of an ethno-medicinal plant inventory. However, before describing in detail this method we illustrate in the following section the aforementioned process by a specific case in Guinea, where ATM is very active.

2.2. Collection of information from a Guinean case study

Our aim is to provide a formal approach for capturing knowledge about ATM and selecting the best medicinal plant for a given disease. To do so, first we need to have a formal model of ATM knowledge and then use this formal model to design a formal selection process of the best treatment of a given disease.

As in many African countries, in Guinea, « modern » a.k.a conventional or occidental medicine is not accessible to the majority of people. Thus, a significant fraction of Guinean people, estimated about 80%, use traditional medicine for their daily care. This is true both for rural and urban areas. For the WHO, the challenge is for any country to encourage local production of herbal medicines and their integration into the healthcare system of the country as this is seen as a way to improve the access to culturally sensitive primary care services.

Guinea has conducted many efforts for promoting effective institutionalization of traditional medicine and integrating it within the global healthcare system. One of the key issues is to present scientific approaches related to the decryption of traditional medical knowledge in order to treat neglected diseases in the country. And the objective is to optimize ATM resources, both tradi-GP and traditional medicines by eliminating harmful traditional practices and highlighting best and reproducible practices and knowledge.

In this context, during the past 10 years, several actions have been conducted. Among them, the National Association of Tradi-GP has been launched. This helped conduct surveys in order to gather information about the vernacular names of diseases, their etiology, their clinical treatment, as well as data related to ritual and prohibitions related to potential treatments. Moreover, in order to facilitate reusing knowledge among the different communities of the country, the University of Conakry elaborated a lexicon of the main medicinal plants used in ATM in the six most spoken languages in Guinea (Kissi, Kpele, Maninka, Fulani, Susu and Toma). Table 1 presents a partial view of this lexicon with the fulani translation. About 800 plants were concerned.

2.2.1. Treatment of malaria (or often widened to fever with icteria) in Guinea (Futah Jallon area)

In the Fuuta Jallon area in Guinea, the following treatments for Malaria are usually prescribed (Table 2). Only the name of the plant and the treatment are indicated. Dosage and frequency of use are not mentioned. According to Table 2, for the treatment of Malaria (or often widened to fever with icteria) various medicinal plants are used in different contexts of prescriptions. These prescriptions depend on the availability of the plants in the considered area and its accuracy depends on some factors. Indeed, the climatic and geographical conditions under which a given plant grows influence the quality of the active ingredients that it contains.

2.2.2. Guinex HTA: an antihypertensive from ATM in Guinea

Many studies highlight the high prevalence of hypertension for Black people, thus for West African citizens. Hypertension is among the 10 priority medical concerns in Guinea and is considered as a real public health problem that requires appropriate responses to the plans of epidemiology and drug therapies (Baldé et al., 2006). The management of hypertension in Guinea in primary care is still inadequate given the lack of epidemiological data, the poverty of populations and inadequate human resources and/ or material resources. This justifies the use of medicinal plants for over 80% of the population (Baldé et al., 2006). In this context, the Centre for Research and Exploitation of Medicinal Plants (CRVPM) launched a program in order to find a treatment of hypertension using traditional medicine. To do so, 98 plants have been studied by the CRVPM and an antihypertensive named Guinex HTA has been provided. It associates the selenium and an extract of *Hymenocardia acida* leaves. Guinex HTA is one of the few drugs from ATM that has received approval to be marketed (Diallo et al., 2012). An extract of the vegetable spices suggested for the treatment of hypertension and collected from traditional medical practitioners and herbalists from three regions of Guinea are listed in Table 3. We have included both the Fulani language and Susu [the language commonly used in the three regions of the study reported in (Balde et al. 2006)] (Table 4).

From the list of 24 medicinal plants, and following the process we described in Section 2.1, the CRVPM has selected the *Hymenocardia acida* associated to the selenium is the best treatment of hypertension. And this is the main component of Guinex HTA.

2.3. ATM knowledge acquisition with the Delphi method

As mentioned previously, ATM domain experts are the most common source of knowledge, with the frequent necessity of collecting knowledge from several individuals. TMPs are interviewed using semi-structured questionnaires with an open-ended informal consultative process that allows conversational communication. The appreciation of the acquired traditional knowledge is made through a participatory assessment of the characteristics of the plant species involved and their traditional medicinal uses. The reality of ATM domain is that any effort will solve only part of the medical problem addressed and must rely on others to reduce the limitations (e.g. unfairness) associated with a single expert's way of reasoning and acting. The potential benefits (e.g. quality of consensus knowledge) of using multiple experts in a knowledge acquisition study generally outweigh potential risks (e.g. difficulties associated with the knowledge merging issues) (Carney, 2007). Group techniques (e.g. nominal group technique and the Delphi technique) for knowledge acquisition studies allow a medical or other decision-making group to resolve complex problems with the focus of generating consensus-based knowledge that is possibly superior to the knowledge elicited from a single expert (Payne et al., 2007). In this work, the Delphi method is used as a knowledge acquisition technique for the elicitation of consensus-based knowledge from domain experts, because it provides anonymity to study participants and generates more regular and stable consensus when compared with other group techniques [e.g. the nominal group technique (Cramer et al., 2008)].

Table 1
Lexicon of medicinal plant and their translation in the Fulani language.

No	Species	Family	Fulani
1	*Acanthhospermum hispidum*	Composaceae	Bulletyaabe
2	*Adansonia digitata*	Bombacaceae	Bhohe
…	…	…	…
798	*Uvaria chamae*	Annonaceae	Boyle
799	*Uvaria thomassii*	Annonaceae	Boylenyaadhu

Table 2
The different ways of malaria treatment in the Fuuta Jallon area in Guinea.

Problem	Name of the plant in Fulani	Scientific name of the species	Prescription
Treatment of malaria (or often widened to fever with icteria) in Fuuta Jallon area	Poore Lammu	*Landolphia heudelotii*	Crush the fruit of *Landolphia heudelotii*, salt and drink
	Sungala, Boyle, Kassia, Kiidi, piya	*Harungana madagascariensis*, *Urena lobata*, *Cassia siamea*, *Jatropha curcas*, *Persea gratissima* or *americana*	Boil, drink and wash yourself
	Nete, Kassia	*Parkia biglobosa*, *Cassia siamea*	Boil, wash yourself and drink
	Jabbhe, Meeko, Kassia	*Tamarindus indica*, *Dialium guineense*	Mix the leaves of *Tamarindus indica*, *Dialium guineense* and thin leaves of *Cassia siamea*. Boil, wash yourself and drink
	Gumbambe	*Cola cordifolia*	Brew the leaves of *Cola codifolia* (fresh or dried) and drink

Table 3
The different way of malaria treatment in the Fuuta Jallon area in Guinea.

No.	Name in Fulani	Name in Susu	Scientific name	Family	Part of the plant used as drug
1	Kiidi	Bakhini	*Jatropha curcas*	Euphorbiaceae	Leaves
2	Pellitoro	Barambaran	*Hymenocardia acida*	Hymenocardiaceae	Leaves
3	Dudukhe	Dundakhè	*Nauclea latifolia*	Rubiaceae	Roots
4	Buudi Darridhi	Fofiya	*Carica papaya*	Caricaceae	Bark of trunk or roots
5	Piya	Piya	*Persea americana*	Lauraceae	Leaves
6	Tombokharii	Maaro nai tyewko	*Albizia zygia*	Mimosaceae	Stem bark, leaves
7	Yorokhoe	Barke	*Piliostigma thonningii*	Caesalpiniaceae	Leaves

Table 4
A description (intent and mappings into CTL) of a response pattern.

Response pattern
Intent: To describe cause-effect relationships between a pair of events/states. An occurrence of the first named the cause must be followed by an occurrence of the second named the effect **Mappings into CTL formalism**: In these mappings, P is the cause and S is the effect • ***Globally***: AG(P ==> AF(S)) • (*) ***Before R:*** A[((P ==> A[!R U (S &!R)]) | AG(!R)) W R] • (*) ***After Q***: A[!Q W (Q & AG(P ==> AF(S))] • (*) ***Between Q and R***: AG(Q &!R ==> A[((P ==> A[!R U (S &!R)]) | AG(!R)) W R]) • (*) ***After Q until R***: AG(Q &!R ==> A[(P ==> A[!R U (S &!R)]) W R]) []= always, < > =eventually,!=not, U=strong until, W=weak until, ==> =implies Equivalences between W and U: A[x W y] =!E[!y U (!x &!y)], E[x U y] =!A[!y W (!x &!y)]

Delphi is described as a structured group communication process that allows a decision-making group to resolve complex problems with the goal of producing useful guidance and opinions for decision makers (Milholland et al., 1973; Linstone and Turoff, 1975; Rowe et al., 1991). The Delphi method (Cuhls, 2003) plans several rounds of questionnaires sent to the different experts involved. The results collected can be included partially in a new round of questionnaires, in order to re-orient the initial problem. This process continues until consensus has been approached among the participants or sufficient information has been obtained.

The Delphi method usually undergoes four distinct phases (Linstone and Turoff, 1975):

(1) Exploration of the subject under discussion, wherein each expert contributes with additional information he feels relevant according to the issue.
(2) Reach an understanding of how the group views the issue, for example, where there is dis/agreement with respect to voting scales like importance, desirability, and/or feasibility.
(3) Exploration of disagreements (if there is a significant disagreement), in order to illuminate the underlying reasons for the differences and possibly to evaluate them.
(4) Final evaluation, which occurs when all previously gathered information, has been initially analyzed and the evaluations have been fed back for consideration.

Delphi can be used to clarify information, elicit consensus-based knowledge and to delineate differences among various experts (Chu and Hwang, 2008). Delphi is particularly useful for knowledge acquisition (Hamilton and Breslawski, 1996) when experts are geographically dispersed because it allows strangers to communicate effectively (Liou, 1992). Delphi has also provided decision support for diagnosis and management of patients, assessed current and future trends in clinical dentistry (Cramer et al., 2008) and it has been carried out to reach consensus among professionals with a specific interest in chronic pain (Mir et al., 2007). In fact, Delphi has been widely used for knowledge intensive activities [including Research & Development, customer service, forecasting, and business performance evaluation, Holsapple and Joshi, 2002; Hayes, 2007; Bryant and Abkowitz, 2007; Nevo and Chan, 2007)].

We argued that a Delphi-based knowledge acquisition process is a reasonable approach for conducting knowledge acquisition in ATM problems, for two reasons (Linstone and Turoff, 2011): (i) it provides a mechanism for reconciliation of conflicts between multiple experts that are asynchronous, and (ii) it facilitates interaction among geographically dispersed individuals in collaborative organizational systems (Linstone and Turoff, 2011). The Delphi method can be incorporated in computer environments for improving the performance of human groups on medical practice and decisions (Turoff and Hiltz, 1996). For instance, Atemezing and his colleagues implement the Delphi process through integration of computer based methods in which there are several agents that represent ATM healers with their expertise in order to reach a consensus for providing a treatment to a patient (Atemezing et al., 2009).

2.4. Knowledge representation models

There is a diversity of knowledge representation languages that include mainly the graph-based approach (e.g. conceptual graphs and semantic networks) and the frame-based approach [e.g. Frames and Descriptions Logics (DLs)]:

- the frame-based approach represents knowledge using an object-like structure (e.g. individual elements and their organized classes) with attached properties. The semantics of frames is not entirely formalized, whereas the fully defined set-theoretic semantics of DLs supports specialized defined deductive services (e.g. knowledge consistency and information retrieval).
- the graph-based approach represents knowledge as labeled direct graphs, where nodes denote conceptual entities (concepts or relations) and arcs the relationship between them. Semantics networks suffer from the lack of a clear semantics, whereas the underlying logical semantics of conceptual graphs provides a diagrammatic reasoning service allowing sentences

that are equivalent to the existential conjunctive positive fragment of first-order logic to be written in a visual or structural form.

The graph-based approach (of which conceptual graphs are a key representative) has advantages over frame-based models in expressing certain forms of modeling (e.g. mapping properties into nested contexts) and in providing a visual reasoning that facilitates an intuitive understanding. In addition, conceptual graphs can be easily translated into the terminology of some other approaches in knowledge engineering, such as RDFS (Yao and Etzkorn, 2006) and its evolution, the OWL (Casteleiro and Diz, 2008; Horrocks et al., 2005) mainly applied in connection with the Semantic Web framework (Shadbolt et al., 2006). As a result, the possibility to interact and exchange the modeled knowledge with internal and external collaborators is provided for various actors of the ATM domain.

In fact, modern terminologies (e.g., SNOMED CT and NCI Thesaurus) are being formalized using Description Logics (DLs) (Baader et al., 2003). Since DLs and CGs are both rooted in semantic networks and logically founded, the question of their relationships has often been asked. As well as similarities between DL and CGs, there are specific interesting features: cycles, *n*-ary relations, and type-hierarchy for CGs; the style of symbolic, variable-free formulas, variety of constructors with different levels of expressiveness for DLs. Besides visual reasoning facilities, the syntactical possibilities of the graphs, including identity, graphs that contain circles, graphs that are not connected, etc., allow graphs to be constructed that do not have counterparts in DL (Dau and Eklund, 2008). However, the conceptual graphs' expressiveness might not be satisfactory for temporal modeling of a given domain knowledge. In order to overcome the aforesaid drawback, in this paper we propose a formal temporal knowledge modeling, which introduces the semantic interpretation of Computational Tree Logic expressions in conceptual graph models. The temporal knowledge modeling is represented by nested conceptual graphs used to describe property specification patterns that formalize the knowledge modeling in the application domain.

After the review of knowledge formalization using the Delphi method and conceptual graphs, we detail in the following section an approach of modeling ATM. To do so, we start by describing briefly the existing resources in the biomedical domain that we have reused for our approach of ATM formal knowledge. A more complete review about ontologies and structured vocabularies in the medical domain can be found in Simonet et al. (2008).

3. Structuring concepts of ATM vocabulary

3.1. Existing drug classifications/terminologies

3.1.1. The EphMRA classification

The EphMRA brings together European research-based pharmaceutical companies operating on a global perspective. The main classification developed by the EphMRA is the Anatomical Classification system (AC-system) jointly with the Pharmaceutical Business Intelligence and Research Group (PBIRG). This classification represents a subjective method of grouping certain pharmaceutical products according to their main therapeutic indication and each product is assigned to one category. There are four different levels in this classification. The first level of the code is based on a letter for the anatomical group and defines 14 groups (A for alimentary tract and metabolism, B for blood and blood forming organs, etc.). The second level adds a digit to the first level and regroups several classes (of the first level) together in order to classify according to indication, therapeutic substance group and anatomical system. The third level adds a letter to a second level code and describes a specific group of products within the second level (according to the chemical structure, indication or method of action). The fourth level adds a digit to the third level and gives more indication on the elements of this level (formulation, chemical description, mode of action, etc.).

3.1.2. ATC classification/DDD

The ATC system proposes an international classification of drugs and is part of WHO's initiatives to achieve universal access to needed drugs and rational use of drugs. Drugs are classified in groups at five different levels and this classification is an extension of the ATC-system. In order to measure drug use, it is important to have both a classification system and a unit of measurement. To deal with the objections against traditional units of measurement, a technical unit of measurement called the Defined Daily Dose to be used in drug utilization studies was developed.

Drugs are classified in groups at five different levels. At the first level, drugs are divided into 14 main groups, with one pharmacological/therapeutic subgroup (second level). The third and fourth levels are chemical/pharmacological/therapeutic subgroups and the fifth level is the chemical substance. The second, third and fourth levels are often used to identify pharmacological subgroups when that is considered more appropriate than therapeutic or chemical subgroups.

Drugs are usually divided in different groups according to the organ or system on which they act and/or their therapeutical and chemical characteristics. Each drug has an English Preferred Name, a list of English synonyms and a list of synonyms in other languages. Each drug has an international common denomination (ICD) proposed by the WHO and has a set of indications, contraindications and side-effects (adverse effects). *Indication* refers to a term describing a valid reason to use a certain test, medication, procedure, or surgery. While *Contraindication* is a condition or factor that increases the risks involved in using a particular drug, carrying out a medical procedure or engaging in a particular activity. Contraindications are divided in two categories: absolute contraindication and relative contraindication. An absolute contraindication is a condition that prohibits the use of a treatment altogether. A relative contraindication weighs in against the use of a treatment when assessing its risk/benefit ratio.

A drug is constituted by at least one active substance and a set of excipients. Each active substance has a proportion in a given drug. A DDD (Defined Daily Dose) is assigned to each drug which has an ATC code (see below). The DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults. The DDD is expressed with a certain unity called DDU (Defined Dose Unit). For the mono composed drugs in general the DDU is generally a weight unit. The DDD for a drug may differ according to the administration mode. Uppsala Monitoring Centre (UMC) has undertaken a project with the aim of attaining global standardization for herbal medicines (Farah, 1998). The scope was to standardize information about herbal medicines, including their scientific names and therapeutic implications, which can vary widely between countries. The structure of the ATC-system, developed for classification of orthodox medicines, was used as a basis for the Herbal ATC structure, and Herbal ATC system remedies are divided into groups according to their therapeutic use. The proposed system for ATC classification of herbal remedies is fully compatible with the regular system (Farah, 2004a, 2004b). Although herbal products are difficult to classify, the UMC try to produce a classification which is both internationally acceptable botanically (names in Latin and vernacular or common names), and medically, as well as being available in a computerized format to link all synonyms (Farah, 2005). The result of the investigation shows that the collected information (including the safety and toxicity data) of herbal medicines are of direct relevance to health professionals and producers of herbal medicines. The Herbal ATC system supports international pharmacovigilance in management and communication for medicine safety activities including adverse reaction monitoring with a potential impact on the known, day-by-day and avoidable damage caused by drug therapy (Farah et al., 2000a, 2000b). When linked to existing information systems, the hierarchical HATC structure supports both the broader overview, and in-depth analysis.

3.2. A proposal for an ATM formal conceptual model

The objective of the research work we conducted falls into two axes: (i) providing a formal model describing African traditional medicine, and (ii) providing a computerized system based on the formal model in order to help efficient decision making. The ATM formal model represented using the Conceptual Graph formalism can be used for different purposes. The first one is conceptual annotation (Patriarche et al., 2005) and semantic indexing (Diallo et al., 2006) of ATM related resources which allow semantic search. Indeed, it is crucial to help medical experts and pharmacovigilance authorities find in an efficient way documents describing processes, methods, etc., related to ATM for better decision making. It has been proven that semantic search provides better recall and precision than keywords-based search. Moreover, as the concepts in the ATM model are denoted by synonym terms in different African languages, it is possible to do cross-lingual retrieval of ATM related resources.

The second purpose is to help performing reasoning from the encoded knowledge in order to find similar patterns between practices and help them inferring sharing and promoting best practices among ATM practitioners. The third purpose is to serve as background knowledge for automated signal generation in pharmacovigilance (Henegar et al., 2006; Bauer-Mehren et al., 2012), in particular ATM dedicated signal generation. Henegar and his colleagues provide an ontology to be used for unsupervised statistical machine learning on spontaneous reporting systems for discovering unknown adverse drug reactions (Henegar et al., 2006); while Bauer-Mehren and his colleagues use different medical terminologies and literature mining (Kamsu-Foguem et al, 2013) for the early detection of drug signals from eight European patient databases (Bauer-Mehren et al., 2012). To the best of our knowledge there is no research work based on a formal model and dedicated to ATM pharmacovigilance.

For instance, by investigating groups of herbal drugs with similar therapeutic, pharmacological and chemical properties it is possible to find out if the adverse drug reaction is caused by a specific herbal product or if it is a group effect (Fucik et al., 2002). The ATC system uses WHO Adverse Reaction Terminology (WHO-ART) that has been developed to serve as a basis for reporting of adverse reaction terms. WHO-ART (WHO, 1992) is a hierarchical structure linking system organ classes to three types of terms: broad "high-level" terms; more specific and disease-related or symptom-related "preferred" terms; and finally the frequently reported alternative "included" term and true synonyms (see an example in Fig. 2).

Note that the system provided is not intended to be directly used by ATM practitioners. Rather, it is intended for researchers or drug regulatory authorities in their tasks of understanding and monitoring adverse drug reactions.

Herbal medicines include herbs, herbal materials, herbal preparations and finished herbal products. In some countries herbal medicines may contain, by tradition, natural organic or inorganic active ingredients that are not of plant origin (e.g. animal and mineral materials) (WHO, 2004). Atemezing and Pavon (2009), the work described presents an ontology that can feed the ATM domain with the particularity of being extendable to other types of traditional medicine. In our modeling, the domain ontology for structuring drug vocabulary appears as a directed acyclic graph. The parent and child terms are connected to each other by *is_a* and *part_of* relationships. The former is a relation in which the child term is a more restrictive concept than its parent. In the conceptual graph formalism, the ontological knowledge is formalized through a structural mapping with a set of mathematical formulas (Sowa, 2000). The formalization underlying the domain ontology provides means to express logical reasoning in order to compare objects described by one or several semantic features (Kamsu-Foguem et al., 2008). So, it is possible to study the ontology structure in order to extract that knowledge that can provide a higher degree of similarity evidence between concepts. For instance, a recent work proposed a new measure of semantic similarity based on the exploitation of the taxonomical knowledge of an ontology, which is able to avoid associated issues (the computational efficiency and resource-dependency aspects) of existing measures and improve their performance (Batet et al., 2011). Such a similarity measure considers all the superconcepts of terms in a given ontology in order to run information retrieval tools with *the advantage of potentially providing accurate information results*. As an application with herbal remedies classification, required knowledge and information about medical use can be found, particularly regarding the monitoring of the adverse effects of drugs.

As described in Fig. 3, the five top-level nodes of a partial view of the ATM Ontology are *Symptoms*, *Medical sign*, *Disease*, *Activity* (treatment or diagnosis) and *dosing devices*. The *Symptoms* includes *General status, Neurological/Psychological, Ocular, Gastro-intestinal, Cardiovascular, Urologic, Pulmonary, Integumentary, Obstetric/ Gynecological, Rheumatism*. The *Disease* includes *Mental* and *Physical illness*. Regarding to the form of *Diagnosis* and *Treatment* (indigenous herbalism and African spirituality), they are classified as sub-concepts of the *Traditional Medicine_Activity* concept. In accordance with both the ATC and the Herbal ATC systems, remedies are divided into groups (cardiovascular system, nervous system, respiratory system, and so on) according to their therapeutic use. The herbal material includes roots, leaves, stems, barks, fruits and seeds. Finally, the dosing devices found in herbal

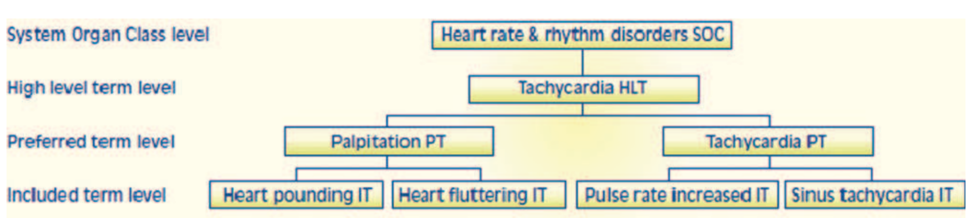

Fig. 2. An example showing the principle of the WHO-ART hierarchy (UMC, 2004).

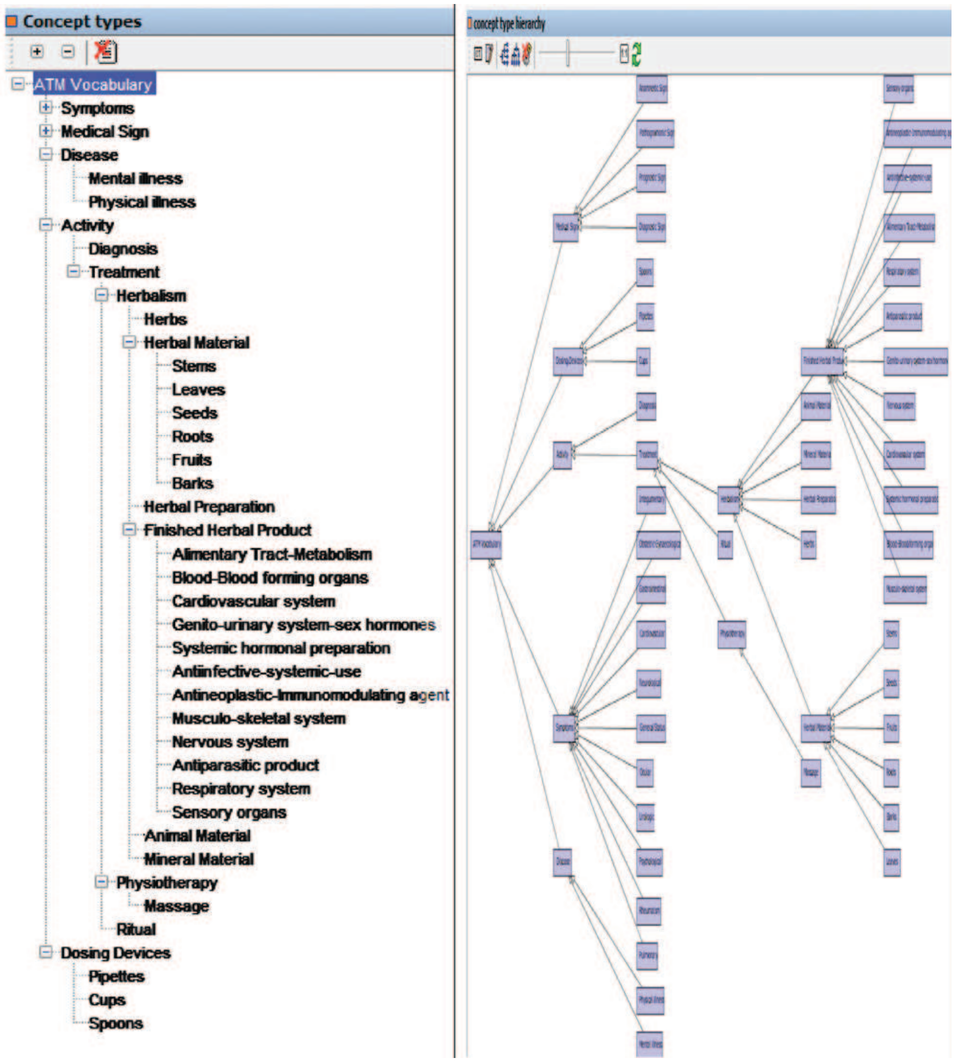

Fig. 3. Partial concept type hierarchy of African traditional medicine (tree view on the left and graph view on right).

oral liquid remedies are medicinal cups, wells and cylinders; medicinal spoons and oral pipettes, droppers and syringes.

In addition, query expansion is made possible thanks to the inferred concepts (e.g. hierarchical subsumption) within the CG based ATM model. For instance, according to Fig. 3, a query for resources related to *Medical Sign* could include resources related to *Anamnestic Sign, Prognostic Sign, Pathognomonic Sign*, etc.

4. Conceptual graphs of specification patterns in the medical context

4.1. Knowledge representation language: conceptual graphs

4.1.1. Informal definition

A conceptual graph is a graph with two kinds of nodes respectively called *concepts* and *conceptual relations* and must meet the following two conditions (Sowa, 1984): (i) each arc must connect a *conceptual relation* to a *concept* (it is said that the graph is bipartite); and (ii) a *concept* that is not connected can form by itself a conceptual graph. Conversely, any relation must be linked to one *concept*.

A concept consists of a type and a referent: the types are partially ordered, the referents are specified by quantification and designations.

The conceptual relationships can be primitive or defined. They form a set R which is equipped with a partial order. They are characterized by their valence, with their signatures and their type. The valence is a positive integer corresponding to the number of edges that may belong to the relation. The signature of a relation r with the valence n is the *n-tuple* $(t_1, t_2,\ldots,t_n)$ of the types of concepts that may be related to r.

These concepts and conceptual relationships are used to describe knowledge bases and the underpinning reasoning is transitive (possibility of inference by inheritance) and well defined. By convention, the rectangles correspond to the concepts and conceptual relations to pseudo-ellipses. The designation of a concept can be a conceptual graph, and this possibility allows modeling the notion of context (Sowa, 2000). Particularly, the proposed representation is a simple mental image of contexts nesting.

4.1.2. Formal definition

A support is a 3-tuple $S=(T_C, T_R, I)$. T_C and T_R are two partially ordered finite sets, respectively, of concept types and relations types. T_R is partitioned into subsets $T_R^1,\ldots,T_R^k$ of relation types of arity $1,\ldots,k$ respectively ($k \geq 1$). Both orders on T_C and T_R are denoted by $\leq$ ($x \leq y$ means that x is a subtype of y). I is a countable set of individual markers describing specific entities. T_C, T_R and I

are pairwise disjoints. All supports also possess the marker*, called generic marker describing an unspecified entity. The set $I \cup \{*\}$ is partially ordered in the following way: * is the greatest element and elements of I are pairwise incomparable. Structuring of concepts both clarifies the knowledge and enables richer descriptions, and hence an ontological form is useful for ATM (Ayimdji et al., 2011). Therefore, we use a first-order logic representation to define classes in a structured way. This representation, for example, permits us to infer that cough is a symptom but also that if a symptom is present it should be at least one of cough, dyspnea, fatigue, or sputum. Symptoms are those things that a patient would report, signs can be measured by a clinician and treatments can be herbalism, physiotherapy or ritual. The logical formula associated to the patient definition type is the following: $\forall p$, *Patient* $(p) \wedge$ *Treatment* $(p, t) \Leftrightarrow$ (*Herbalism* $(p, t) \vee$ *Phisiotherapy* $(p, t) \vee$ *Ritual* (p, t)).

A simple Conceptual Graph G, defined over a support S, is a finite bipartite multigraph ($V=(V_C, V_R)$, E, L):

- V_C and V_R are the node sets, respectively, of concepts nodes and of relations nodes.
- E is the multi-set of edges. Edges incident to a relation node are totally ordered.
- Each node has a label given by the mapping L. A relation node r is labeled by type(r), an element of $T_{R,}$ and the degree of r must be equal to the arity of type (r).
- A concept node c is labeled by a pair (type(c), marker(c)), where type(c) is an element of T_C called its type, and marker (c) is an element of $I \cup \{*\}$.

Projection operation is the key computational notion for reasoning on conceptual graphs, since it corresponds to the logical subsumption when considering the logical formulas associated with conceptual graphs. Projection can be seen as a global view of a specialization operation sequence. From an algorithmic viewpoint, the computational problem of determining whether a given graph can be projected in another graph has a nondeterministic polynomial time (Mugnier, 1995). Some polynomial cases are obtained by restricting the form of the graphs in practical applications, especially with a polynomial that depends on the choice of query graph (Baget and Mugnier, 2002). For instance, the projection of an acyclic conceptual graph into another graph is polynomial.

4.1.3. *Formal visual reasoning*

Projection is the basic mechanism of reasoning in conceptual graphs (Chein and Mugnier, 2008). It replaces the logical implication of information retrieval by a process of graph specialization. Thus, one can notice that the projection operation defined in the conceptual graphs can be used in information retrieval in order to improve accuracy (e.g. use of structures typing) and conceptual ancestor recall (e.g. use of logical implications resulting from the subsumption of types). As the saying goes "a picture is worth a thousand words", the conceptual graph operations are a wonderful means for the democratization of logical reasoning (mainly deduction and abduction). Without ruling out the demonstrations by the logical formulas, graph operations are sufficient to explain the reasoning process like a diagram that could serve as proof of demonstrations until a better control of logical tools (Chein et al., 2013). Often in several cases, a sequence of suitable graphic illustration is sufficient in itself to reach a solution. It arouses somebody's intuition rather than theoretical knowledge, sometimes fragmented and inefficient.

During a formal verification process (Kamsu-Foguem and Chapurlat, 2006), it has to be proved that the ATM knowledge does not contain only the potential incoherencies and inconsistencies intrinsic to the cultural beliefs underlying the ATM domain, but it also ensures respect for different types of temporal properties useful for the effective implementation of this ATM knowledge. The verification procedures are fully graphical since all knowledge is represented by conceptual graphs and all the reasoning mechanisms are performed by graph operations (based mainly on the projection). This allows visualization of the reasoning and the use of structural properties of graphs to verify compliance of the ATM knowledge in relation to requirements (good medical practice, cultural characteristics, objective of the ATM protocol and patient clinical status). The mechanism of projection performs a specialization calculus between graphs that reflects the specialization relationships described in the concepts, relationships and temporal modalities hierarchies. In other words, one verifies that a graph G_1 modeling a property is a specialization of G_2 modeling a part of the ATM protocol if and only if there exists a projection of G_1 in G_2 such that all concepts and relationships nodes of G_2 are projected on nodes of G_1 whose type is the same or a specialization according to the specified hierarchical vocabulary.

More formally, let Q and G be two simple conceptual graphs defined on a support S. A projection from Q to G is a mapping Π from the set $V_C(Q)$ of concept nodes of Q to $V_C(G)$ and from the set $V_R(Q)$ of relations nodes of Q to $V_R(G)$ that respects their structure. It is a bipartite graph homomorphism, which maps adjacent nodes to adjacent nodes and offers the possibilities of specialization of the concept and relation nodes labels. More formally, this mapping has these two properties:

- $\forall (r, i, c) \in E(Q)$ the set of edges of Q, $(\Pi(r), i, \Pi(c)) \in E(G)$;
- $\forall x \in V_C(Q) \cup V_R(Q)$, label $((\Pi(x)) \leq$ label (x).

Practical understanding of this is that projection operation can be applied to graph checking by searching for an occurrence of a source graph in a target graph, so it is possible to obtain proofs of some properties of queries.

4.2. *Conceptual graphs for representing temporal knowledge*

The ATM guidelines express temporal dynamics (e.g. first prescribe drug A, if that fails prescribe drug B), which is cumbersome to describe in first-order predicate logic. In general, medical monitoring will result in temporal expressions, thus a representation over time is necessary. The advantage of the temporal logic representation is the clear interpretation and concise knowledge base. The temporal knowledge base (KB) from the ATM guidelines can be used to make recommendations about suggested drugs based on medical literature, each of them with a level of confidence. However, the recommendations may be disregarded in specific cases if there are clinical reasons to do so according to the treating ATM practitioner and adverse drug reactions.

There are certain cautions and limitations of conceptual graphs for representing temporal knowledge: for instance, the ambiguity and incompleteness of temporal information specification with the provided contextual structures in knowledge representation models. An extension as a framework for modeling temporal knowledge in natural language processing has been proposed by Moulin (1997). In particular, he has developed some procedures for verb tense determination in order to understand the temporal structure of a discourse. Our aim is to provide a semantic representation scheme integrating the main features of a temporal logic perspective thanks to the introduction of temporal operators that may be nested at various levels, creating temporal contexts.

4.2.1. *Formal definition of nested conceptual graphs*

Like the simple conceptual graphs, nested conceptual graphs are defined on a support S. However, the label of a concept vertex now has three fields, we denote (t, m, d). The fields t and m are, respectively, the type and marker as defined previously. The third field, called internal partial description, corresponds to more specific information related to different kinds of contextual facts. This field can be either equal to **, the generic description, or a graph. Nested Conceptual Graphs (NGs) are defined by structural induction as follows:

(1) A simple conceptual graph, which has completed all the label of each concept node c, by a third field **, is a basic NG (i.e. a NG of level 0).
(2) Let G be a basic NG, let $c_1, c_2, \ldots, c_k$ be concept nodes of G, and let $G_1, G_2, \ldots, G_k$ be NGs. The graph obtained by substituting G_i to the description ** of c_i for $i=1, \ldots, k$ is a NG. If the maximum level of G_i is k, then the level or depth of G is $k+1$. A node of G with a non-empty description is called a *complex* node.

Considering the fact that the graph operations formalize reasoning, the notion of projection is actually extended to nested graphs, by induction on the depth of a considered query graph. Nested allow one to represent hierarchically structured knowledge, and projection allows one to reason at specific levels.

4.2.2. *Formal definition of projection for nested conceptual graphs*

A projection from NG G to a NG H is a family of mappings $\Pi = \Pi_0, \Pi c_i, \ldots \Pi c_k$, where $c_1, c_2, \ldots, c_k$ are the complex nodes of G, which satisfies:

(1) Π_0 is a projection from the simple conceptual graph associated to the root of G to the simple conceptual graph associated to the root of H.
(2) For all c_i complex node of G_i, $\Pi_0(c_i)$ is a complex node of H and Πc_i is a projection from the NG description of c_i to the NG description of $\Pi_0(c_i)$.

Nesting shows that an inductive variation of the typical projection operation constitutes the inference motor for nested graphs. This separation of level of reasoning increases efficiency and clarity when extracting information (Genest and Chein, 2005).

Logically dividing a single complex graph into several consistent annotated units can make it easier to understand. Target professionals, guided by structural annotative information, can successively focus on the different parts of the graph, and finally have an easier global comprehension of the modeled knowledge (Jouve et al., 2003).

Note that the predicate to internal description takes a formula as argument. Thus this logical semantics goes beyond First-Order Logics. For instance, a non-classical semantics equivalent to NG homomorphism has been introduced (Preller et al., 1998). Meanwhile, to the best of our knowledge and belief, the approaches contained in the published works of conceptual graphs community cannot enable us to explicitly model temporal situations. Although not directly addressed in the scientific literature, further efforts are necessary to achieve the temporal representation's objectives, in particular in the area of traditional medicine where the core disciplines for research and application include ethnomedicine, ethnobotany, and medical anthropology. We propose an approach which can be used to formally represent the temporal knowledge contained in medicinal product information. By adding to simple conceptual graphs a description representing temporal operators, one obtains the means to represent temporal knowledge as in temporal language like from Computation Tree Logic (CTL) (Clarke et al., 1986). These temporal operators control the semantics of temporal descriptions which are defined in nested temporal graphs. The extended projection remains an inductive variation of the typical projection operation that allows a specialization of the vertices labels, except that this specialization integrates now temporal descriptions of nested graphs.

4.3. *Property specification patterns*

A property specification pattern is a generalized description of a commonly occurring requirement and it describes widespread types of temporal properties with their associated formal expressions (Dwyer et al., 1998). The works of Dwyer et al. (1999) provide a collection of simple patterns defined to assist practitioners in mapping descriptions of temporal properties into formal languages [e.g. various temporal logics, such as Linear temporal logic (LTL) and computation tree logic (CTL)]. In their approach, the patterns are organized in a semantic hierarchy distinguishing properties that deal with the occurrence (e.g. the *Absence* pattern) and others constraining the order of states/events (e.g. the Precedence pattern). Furthermore, each pattern has a scope (Fig. 5) that specifies the extent of the program execution over which the pattern must hold. There are five basic kinds of scopes (Dwyer et al., 1998): *global* (the entire program execution), *before* (the execution up to a given state/event), *after* (the execution after a given state/event), *between* (any part of the execution from one given state/event to another given state/event) and *after-until* (like between but the designated part of the execution continues even if the second state/event not occur). Dwyer's property specification patterns hierarchy has been extended (Fig. 4) with four new subcategories of the *Existence* pattern (*Everywhere eventually, Possible existence, Always eventually* and *Liveness*) (Ryndina and Kritzinger, 2005). The work of Awad et al. (2011) introduces compliance patterns on *precedence* to *conditional activity execution*, *conditional before-scope absence*, and *conditional between-scope absence*.

Each pattern comprises a name, a precise statement of the pattern's intent; mappings into common specification formalisms. As example, we present the *response* pattern in Fig. 5.

4.4. *Graph-based specification for traditional medicine*

The goal of this part is to provide a framework to enable the identification of different requirement sources on which ATM properties are expected to hold, enabling non-experts to easily write formal specifications. Based on these requirements, the idea is to establish a set of property specification patterns which provides complete support for the formal specification of commonly occurring properties associated to good medical practice and the patient specific clinical condition. Then, each property formulated in natural language in a specific requirement source background conforms to one of the defined patterns. Such

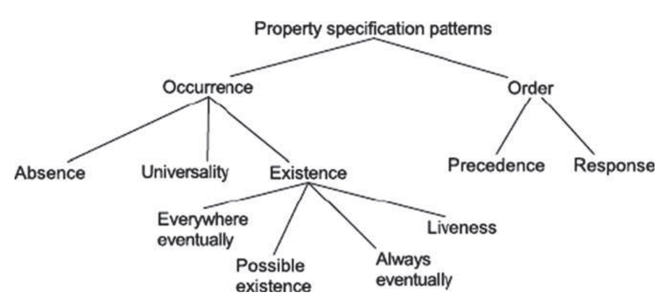

Fig. 4. Ryndina's property specification patterns hierarchy.

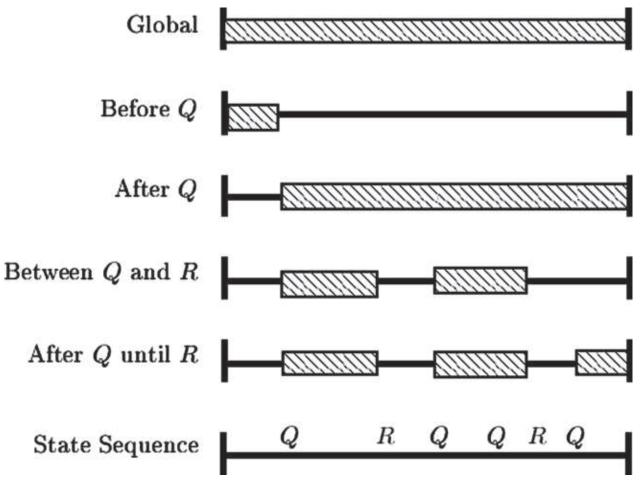

Fig. 5. Pattern scopes.

patterns, by providing the mappings of the property to formal specification languages enable users to easily formulate the requirement to be checked against the ATM guideline. Recently, researchers have used temporal logic as a formalism to capture the temporal nature of knowledge available in clinical guidelines (Hommersom et al., 2007; Pérez and Porres, 2010). This allows reasoning with the represented knowledge for different purposes. Examples include checking formal properties such as whether particular treatment prescriptions are correct. We believe that such logical formalizations offer a good starting point for the formalization of knowledge related to ATM practices that are fraught with issues of imprecise dosage, poor diagnosis, and inadequate knowledge of anatomy (Hillenbrand, 2006). These issues put patients' health and lives at risk (Shetti et al. 2011). So one would expect that a good-quality medical guideline regarding treatment of a disorder would preclude the prescription of redundant drugs, or advise against the prescription of a treatment that is less effective than some alternative (Pérez and Porres, 2010). Such requirements aim at verifying whether the ATM practitioners follow good medical practice. Since principles of best care practice become a medical standard for optimal care, the defined properties can be as far as prescribed treatments, medical actions to be carried out, etc., are concerned.

As shown in the previous section, Dwyer et al. have proposed to capture the experience of the expert and enable the transfer of that experience between practitioners by a specification pattern system. This system is essentially a collection of parameterizable, high-level, formalism-independent specification abstractions organized into one or more hierarchies, with connections between related patterns to facilitate browsing (Dwyer et al., 1998). In practical situations, the formal version of the requirement specification is an instantiation of a template mapping for a specific pattern/scope. A user would search for the appropriate pattern to match the requirement being specified, use the mapping section to obtain a template of the property in the formalism used by a particular tool, and then instantiate that template by connecting in the state formulas or events specific to the requirement.

We want to establish a mapping from patterns to conceptual graphs and back to alternative formal formalisms (e.g. LT or CTL). In this manner, a user wishing to search for the appropriate pattern to match the requirement being specified is able to obtain the essential structure of the pattern in the conceptual graph formalism. In their initial description made by John Sowa, the expressive power of conceptual graphs was limited with equivalence to first-order logic. Thus, extensions have been proposed to allow the representation of the temporal contexts, including in the expression of temporal discursive terms (Moulin, 1997) (Chu and Cesnik, 2001). In this case, the principle of nesting conceptual graph was used to provide a graphical representation of specification patterns. It is in this context that our work takes place and we provide some examples of mappings from conceptual graphs to CTL for certain pairs of patterns and scopes.

TM must strive towards good medical practice, which is defined by scientific knowledge, practical experience and professional acceptance. Previous works (Hommersom et al., 2007; Pérez and Porres, 2010) have identified the different types of knowledge that are involved in defining quality requirements useful for good medical practice. These requirements help to determine some property specification patterns of commonly occurring medical situations. Each property expressed in natural language in a particular requirement source background is related to one of the defined patterns.

Each pattern is visually represented as a Conceptual Graph, has a defined mapping to an equivalent Computational Tree Logic (CTL) formula. *Precedence* says that some cause precedes each effect, and *Response* says that some effect follows each cause. The *Absence* pattern is the dual of the *Existence* pattern. *Precedence* and *response* properties often go together. A *response* property says that when S occurs then an occurrence of P must follow. If we want to restrict P to only follow S then we use a *precedence* property:

(a) Practitioners have to obtain and analyze the adverse medicinal drug profile (Fig. 6).
  - *P1*: This property is identified as a *Global-scope response* pattern and the corresponding CTL formula is: AG (*P* $==>$ AF(S)).
    - *AG* (*Executed* (*Practitioner prescribes a medicinal drug*)) $==>$ *AF* (*Executed* (*Analyze Adverse Medicinal Drug Profile*)).

(b) *P2*: If the drug safety assessment fails, it must be added to a blacklist (management includes withdrawal of the drug).
  - P2 is identified as a *conditional Response pattern* and the corresponding CTL formula is depicted in Fig. 7.
    - AG (executed (Conduct adverse reaction study) $\wedge$ state (Evaluation, failed) $\wedge$ AG ($\neg$state (Evaluation, passed)) $==>$ AF (executed (Add Involved Drug to Black list)).

(c) Treatment of a disorder would preclude the prescription of redundant drugs, or advise against the prescription of a treatment that is less effective than some alternative (Fig. 8). P3: This property is identified as a *Global-scope Response* pattern with corresponding CTL formula: AG (P $==>$ AF(S)).
  - An occurrence of the ineffective treatment, must be followed by an occurrence of the alternative treatment.
    - *AG* (*Ready*(*ineffective treatment*) $==>$ *AF* (*Executed* (*alternative treatment*)).

5. A case study from Cameroonian traditional practitioners

5.1. Example of effective herbal medicines

In this section, we report on a significant set of effective medicinal plants collected at the Cameroonian Institute for Medical Research and Medicinal Plants Studies (IMPM). The practice of traditional medicine in the urban environment is evolving, influenced by the proximity and availability of health-care centers and pharmacies. For instance, most urban TP use conventional medicine facilities including medical tests for a diagnosis and/or a post-treatment checking (Hillenbrand, 2006). With the legalization of traditional medicine as a complimentary health-care service to primary health care in Cameroon, the role of the traditional healer is essential in the national public health

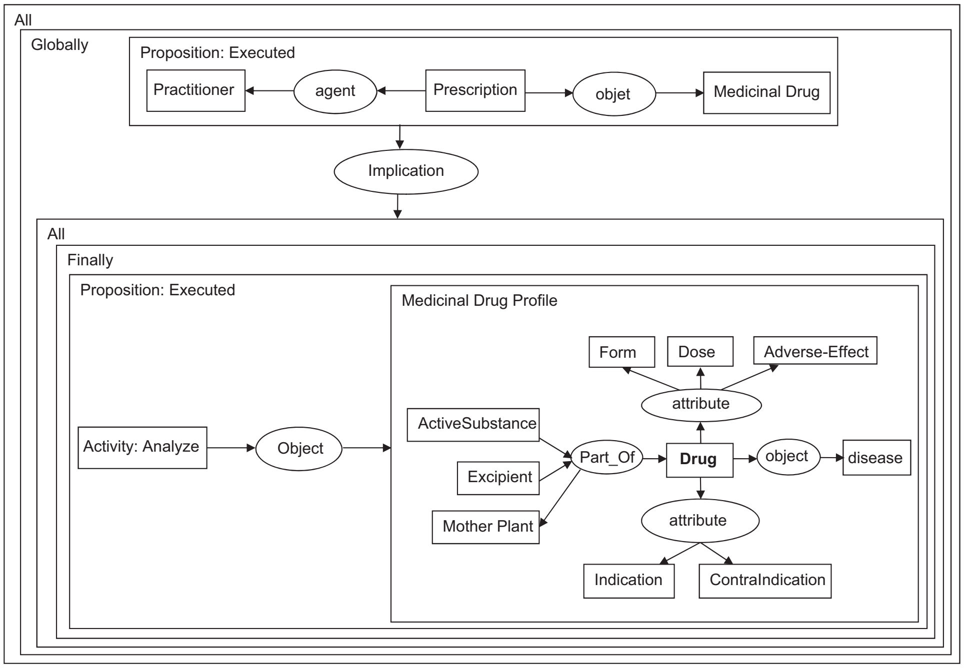

Fig. 6. Graph-based specification of a property related to medicinal drug profile.

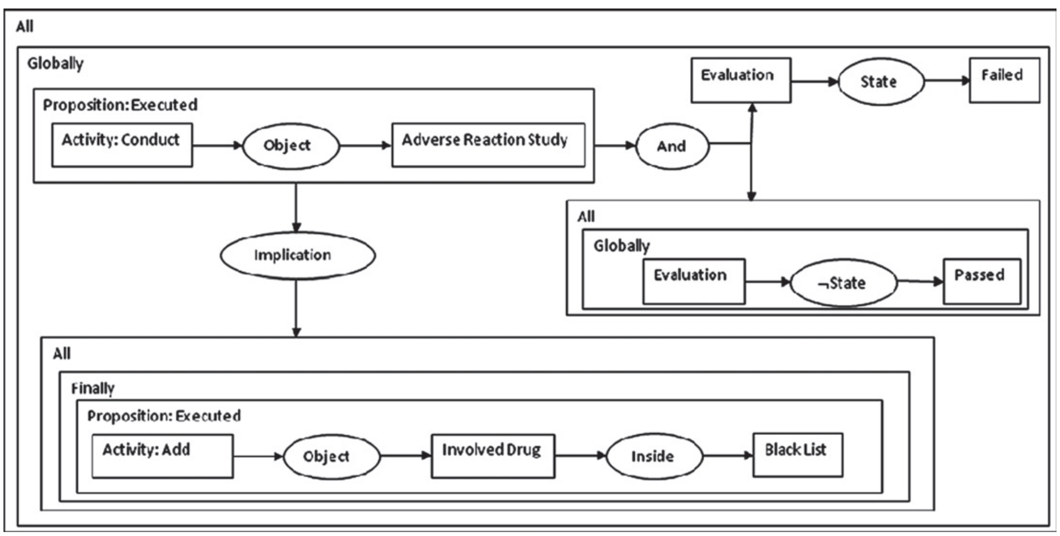

Fig. 7. Graph-based specification of a property related to drug safety assessment.

strategy (Agbor and Naidoo, 2011). Cameroon has carried out inventories of medicinal plants and a monograph on medicinal and aromatic plants has been developed. A number of medicinal plants have showed potential of therapeutic benefits and contribute strongly on the health of Cameroon people. We have identified seven locally available plant species that could be used to treat some disease symptoms. They are described in Table 5. Examples of those medicinal plants include *Codiaeum variegatum* (treatment of amebiasis), *Anacardium occidentale* (treatment of diabetes mellitus), *Dysphania ambrosioides* (treatment of anxiety and fever),and *Tulbaghia violacea* (antithrombotic, anticoagulant and anticancer properties).

5.2. Selection of medicinal plants

Some of the sections in the Cameroonian monograph cover safety data, therapeutic indications and therapeutic actions. Such information is important in the selection of medicinal plants that would be genuine natural alternatives to synthetic chemicals. The most valuable medicinal plants are selected and prioritized in order to encourage the development of methods for the safe and effective use of these medicinal plant products. For instance, one can put them in an education scheme for effective contribution of traditional medicine to mainstream healthcare (Table 6).

Going back to the case study described previously, in most cases, during conceptual representations of existing nomenclatures, there is a difficulty in approaching the implicit meaning and inferences between the different parts of medical speech. Conceptual graphs provide a general framework for encoding knowledge through annotations that are built from an ATM ontology (composed of hierarchies of concepts, relations and nesting). Reasoning is performed by graph operations for annotation base interrogation and answer visualization (Chein, 2009). These graph operations include approximate search and relevance ranking of

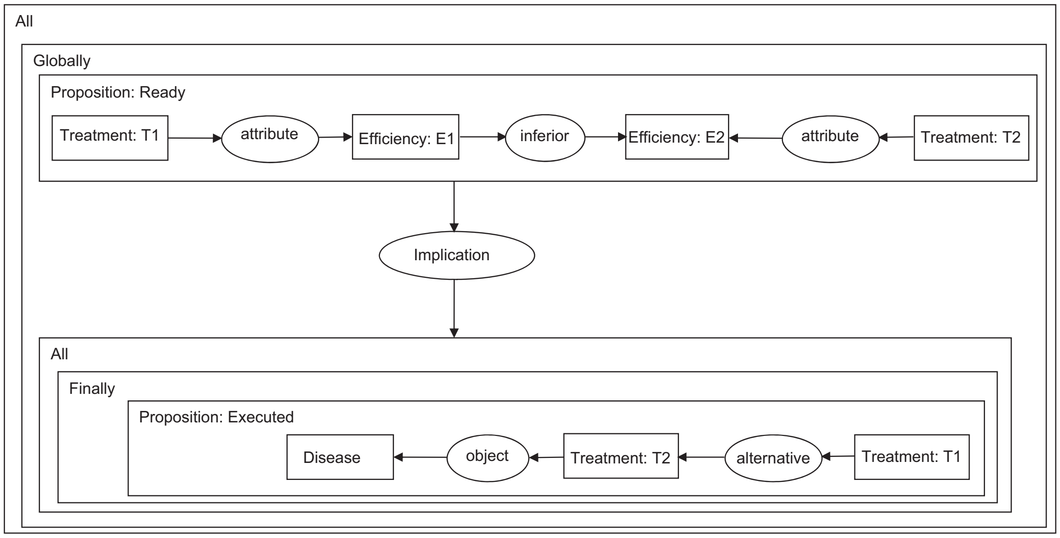

Fig. 8. Graph-based specification of a property related to alternative treatment.

Table 5
Some medicinal plants used in Africa in physical (and mental) disorders.

Plant	Family	Traditional use	References
Pygeum africanum (*Prunus africana* a bark extract)	Rosaceae	A cure for mild-to-moderate benign prostatic hyperplasia	Helwig (2010)
Codiaeum variegatum (leaves extract)	Euphorbiaceae	Treatment of amoebiasis (a gastrointestinal infection) with prevention of induced liver disorders and intestinal ulcers.	Moundipa et al. (2005) and Ogunwenmo et al. (2007)
Anacardium occidentale (hexane extract)	Anacardiaceae	Treatment of diabetes mellitus and prevention of diabetic nephropathy (improvement of renal morphology and function)	Tedong et al. (2006)
Dysphania ambrosioides (formerly *Chenopodium ambrosioides*)	Amaranthaceae	Treatment of anxiety and fever (anxiolytic-like and antipyretic activities)	Ngo Bum et al. (2011)
Millettia thonningii	Fabaceae	Treatment of epilepsy and insomnia	Okomolo et al. (2011)
Crinum glaucum	Amaryllidaceae	Treatment of cognitive impairment symptoms (e.g. memory loss) associated with neurodegenerative diseases (e.g. Alzheimer's disease)	Hostettmann et al. (2006)
Tulbaghia violacea	Amaryllidaceae	Androgenic, antithrombotic, anticoagulant and anticancer properties	Bungu et al. (2008) and Thamburan et al. (2009)

Table 6
Comparison with other approaches using CGs in biology and medicine.

System	Research questions	Used reasoning	Domain
Virtual staff (Dieng-Kuntz et al., 2006)	How to build or enrich an ontology from a structured database?	Logical reasoning	Conventional medicine
EsCorServer (Medina Ramírez, 2007)	How to offer ontology-guided information retrieval?	Logical reasoning	Biology
MEAT (Khelif et al., 2007)	How to create semantic annotations (concepts or relations) semi-automatically from texts?	Logical reasoning	Biology
MIEL (Haemmerlé et al., 2007)	How to perform microbial risk assessment in foods from experimental data?	Fuzzy reasoning	Food microbiology
Our approach	How to provide a computerized system based on the formal model in order to help efficient ATM decision making?	Temporal logical reasoning	Traditional medicine (warning on harmful traditional practices and highlighting best practices with underlying knowledge)

treatment related information in traditional medical practice. In our study, information retrieval is applied to medicinal plants selection in the ontological structure. This selection is based on a semantic similarity measure (Batet et al., 2011) aiming to retrieve the most effective medicinal plants in the treatment of disease concerned.

Finding information about a disease (e.g, gastrointestinal disorders, diabetes mellitus and cancer or cardiovascular diseases), the drug ontology may provide information about drugs (*Codiaeum variegatum*, *Anacardium occidentale* and *Tulbaghia violacea*) and their dosages. Also it may be possible to identify side-effects, indications and contraindications and possibly retrieving documents about these items from the ATM knowledge:

- Providing definition of the ontological aspect which explains the types of entities or classes that are expected to see in a specific pharmacovigilance process.

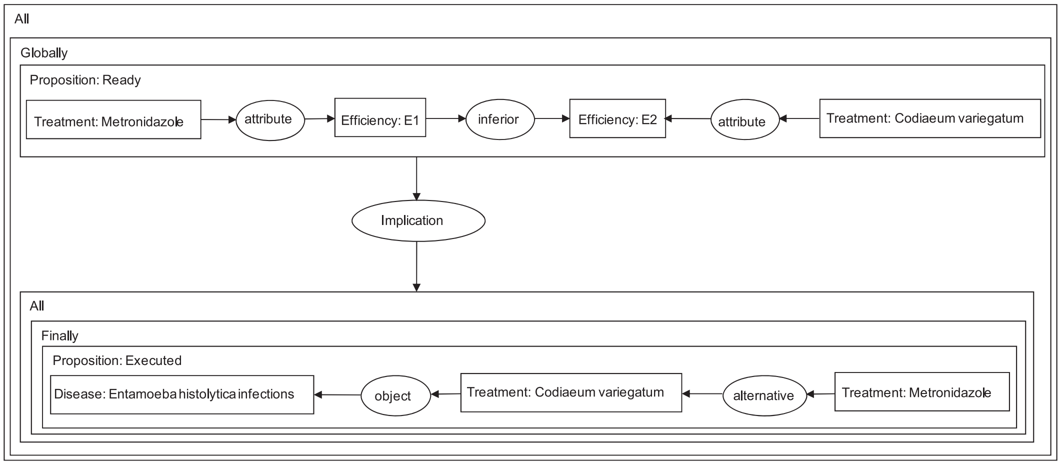

Fig. 9. Graph-based specification of a property related to effective drug substitution.

- Retrieving documents describing the knowledge about safety monitoring of medicinal products and their genuine use in quality and accuracy conditions, and more effective in appropriate contexts.
- Exploring semantic relationships from a drug regarding taxonomic (vernacular, botanical and chemical) identification and querying the ATM database according to the entities selected.

In many situations, the ATM methods of treatment are effective and less invasive in certain cases, as they make use of local herbs and medicinal plants. We can select species of medicinal plants whose effectiveness level of products with the current disease problem is deemed sufficient. Throughout the course of the studies referenced in Table 5, it was reported that the cited medicinal plants exhibited biological activities which were comparable to pharmaceutical drugs. Particularly, *Codiaeum variegatum* exhibited a clear antiamoebic activity for the treatment of *Entamoeba histolytica* infections occurring in the intestine and/or liver, and had a more pronounced activity than *metronidazole*, the reference drug product (Moundipa et al., 2005). In addition, *Tulbaghia violacea* exhibited antithrombotic activities which were higher than those found in *garlic* the reference drug product (Bungu et al., 2008). Both *Codiaeum variegatum* and *Tulbaghia violacea* are alternative medicines that improve informal health services and may contribute to pharmaceutical applications.

In accordance with property specification patterns, graph-based specifications (described with temporal logic formalization in Section 4.4) are instantiated on concrete cases of traditional medicine uses. For instance, the conceptual graph of Fig. 9 has the following meaning: "An occurrence of a less efficient treatment (the efficiency attribute of Metronidazole is lower than the efficiency attribute of the *Codiaeum variegatum*), must be followed by an occurrence of the alternative treatment [alternative medicine with the *Codiaeum variegatum* for Entamoeba histolytica infections (e.g. Amebiasis, amoebic liver abscess and amoebic lung abscess)].

5.3. Practical deployment considerations

Therefore, the idea described in the paper leads to concrete applications: (i) detection of some adverse drug reactions applied to the ATM domain with collaboration of drug regulatory authorities and research scientists interested in clinical research and pharmacovigilance for improving patient safety; (ii) educational purposes addressed to the ATM practitioners thanks to the knowledge formalized within the formal model expressed with the Conceptual Graphs; (iii) managing ATM related resources by semantically annotating and indexing them in order to perform semantic information retrieval; (iv) allowing researchers to identify required information more efficiently; (v) discover new additive and synergic effects of ATM drugs; and (vi) bridge the gaps between Western medicine and ATM.

Furthermore our idea is based on the fact that an intensive effort has been conducted in developing standard medical terminologies, structured vocabularies and other structured vocabulary for western medicine and formalizing knowledge about drug related adverse reactions. This is the case of MedDRA (Brown et al., 1999), the WHO Adverse Reactions Terminology (WHO-ART),[1] the International Classification of Disease (ICD),[2] SNOMED-CT (Cornet and de Keizer, 2008) and the MeSH thesaurus.[3]

MedDRA stands for Medical Dictionary for Regulatory Activities. It is a clinically validated international medical terminology used by regulatory authorities and the regulated biopharmaceutical industry throughout the entire regulatory process, from pre-marketing to post-marketing activities, and for data entry, retrieval, evaluation, and presentation. SNOMED CT (Systematized Nomenclature of Medicine—Clinical Terms) is a systematically organized computer processable collection of medical terms providing codes, terms, synonyms and definitions covering diseases, findings, procedures, microorganisms, substances, etc. The primary purpose of SNOMED CT is to support the effective clinical recording of data with the aim of improving patient care. SNOMED-CT has been widely adopted as a standard for formulating medical concepts. In the 2010 international release of SNOMED-CT, more than 291,000 active concepts are included and the descriptions of these concepts are over 758,000. The concepts are organized into hierarchies, in which 823,000 relationships enable the consistency of data retrieval and analysis.

The WHO-ART is a dictionary meant to serve as a basis for rational coding of adverse reaction terms. The system is maintained by the Uppsala Monitoring Centre (UMC).

As mappings have been provided for the most of above mentioned resources, in particular, under the umbrella of the UMLS (Unified Medical Language System; Humphreys and Lindberg, 1993), it becomes therefore possible to provide mappings between the entities modeled within the ATM formal model and these resources in order to facilitate information and

1 http://www.umc-products.com/graphics/3149.pdf.
2 http://www.who.int/classifications/icd/en/.
3 http://www.nlm.nih.gov/mesh/.

knowledge sharing, but also benefiting from the progress achieved with these standards.

For instance let us take the case study from Cameroonian Traditional Practitioners reported in the previous Section. If we consider the traditional plant *Codiaeum Variegatum* used in Cameroon for the treatment of *Amoebiasis*, and presents in the ATM formal model, we can identify all the declared mappings between this particular disease and the possible corresponding concepts within SNOMED-CT by using the BioPortal repository[4] which includes more than 300 biomedical ontologies, most of them coming from the UMLS resource. Thus *Amoebiasis* is mapped to SNOMED-CT concepts including *Amebic dysentery*, Infection due to *Entamoeba histolytica*, Disease due to *Entamoebidae*. Therefore, it becomes possible to use the mappings between these concepts and those from MEdDRA for instance to infer the known adverse drug reactions due to *Codiaeum Variegatum* in western medicine. Due to the importance of this topic, the World Wide Web Consortium has launched the Semantic Web for Health Care and Life Sciences Interest Group (HCLSIG)[5] with a use case dedicated to Alternative Medicine.

From an implementation point of view, some graph-based programmes of the system which allow adapted information retrieval and comprehensive answers to the most common types of questions have been developed in the CoGui[6] software tool. The main components of CoGui are: (i) the data language for representing ATM information composed of nested graphs, (ii) the query language for searching Nested CGs bases, also based on nested type graphs, (iii) answers are computed by graph operations, and (iv) a graphical user interface. It uses the graph-based operations built into the CGs base and is formulated for the therapeutics and pharmacovigilance purposes. The software allows inference mechanisms and consistencies checking to pinpoint what is important and understand it clearly. For instance, investigating a possible drug–adverse drug reaction relationship put traditional practitioners in a position of being able to make coherent, informed decisions, reducing the safety risks or limitations of use, for the benefit of patients. The pattern of the adverse effect may fit the known pharmacology or allergy pattern of one of the suspected medicines, or be intrinsically linked with specific diseases. The paper of Baget et al. (2009) examines two different translations between RDF(S) (Resource Description Format) and Conceptual Graphs (CGs). These translations will allow tools like Cogui and Cogitant[7] (http://cogitant.sourceforge.net/) to be able to import and export RDF(S) documents. The first (not visual) translation is sound and complete from a reasoning view point, whereas second (visual) translation does not apply to the whole RDF(S).

5.4. Discussion

Knowledge about the effects on health for many medicinal substances included in ATM products is still sketchy, expressly if one takes the possible synergistic effects of the different mixtures into account. Overall, knowledge of adverse drug reactions, such as substance intolerance and hypersensitivity, is important for both practitioners and patients. It is all more useful in traditional medicine, as very few adverse drug reactions of ATM products are measured by well-known indicators. Thus, the understanding of these side effects would be rigorous requirements for the prescriptions that specify the terms and conditions for administering the food supplements and medicinal products. This knowledge will provide an opportunity to verify the clinical appropriateness of the medication delivery processes in order to increase efficiency and improve patient safety. There have been reports of renal failure secondary to dehydration due to nausea, vomiting and associated with adverse drug factors such as inappropriate or concomitant medications including ATM products.

Therefore, the logical assessment of the ATM prescriptions according to possible drug interaction and the patient conditions is a crucial need. Conceptual Graphs formalism can help to solve such an issue. A visual reasoning through CG facilitates this process and could contribute to maintain the natural ties between bioinformatics research and the ancestral practices. The know-how is getting lost, since traditional knowledge is often ignored by the young generations. Meanwhile, ancestral practices and traditions insure the building up of superior cultural relationships and of enduring cultural groups, all of which facilitated the resulting factors in the preservation of civilization. It also important for ATM practitioners who commonly describe medical information with learning opportunities associated to their communication styles. In fact, they habitually use language creatively (symbolisms, metaphors, imagery, etc.) to develop well detailed responses relating to human disease and health (diagnosis, characterization, monitoring, and treatment).

In the trend of using Conceptual Graphs, we provide, in Table 6, the summary of the comparison of our approach with others which use CGs in a similar way. In particular, we have especially addressed related works concerning the biomedical domain reported in the literature (Dieng-Kuntz et al., 2006; Haemmerlé et al., 2007; Khelif et al., 2007; Medina Ramírez, 2007). Our initiative distinguishes itself from these works as their accent lies solely on the logical organization of reasoning. Indeed, contrary to the above reported research work, our approach includes a temporal reasoning processing and a pharmacovigilance orientation for the early warning of possible harmful traditional practices and highlighting best practices with underlying knowledge. This guidance perspective provides an introduction to understanding the knowledge dimensions of practices existing and working in ATM settings. Accordingly, many ATM health centers will successfully adopt standardized dosing and medication delivery processes to facilitate efficient monitoring of ATM products (herbal remedies or supplements).

6. Conclusion and future works

In some situations, traditional medical practitioners use plants that can later be adapted to some feasible pharmaceutical uses with the aid of scientific evidence on the effectiveness (e.g. anti-leukaemia drugs extracted from the Madagascan Periwinkle (*Catharanthus roseus*) or anti-drepanocytosis medicine FACA (a combination of Fagara xanthoxyloides and Calotropis procera from Burkina–Faso, Ouattara et al., 2009). Traditional medicine knowledge management needs to include a minimum requirement set for the efficient practice of traditional medicine. Some major challenges facing the development and use of traditional medicines in the developing countries are related to inadequate information on scientific and clinical validation of many traditional medicines practices (e.g. poor modes of prescription). Owing to the complexity of medicinal plants in particular, it is essential that they are subjected to detailed scientific evaluations, like conventional medicines in order to guarantee their safety, quality and efficacy. This contributes to an effort to make traditional medicine "safe, efficacious, affordable and available to the vast majority of African people" (Kofi-Tsekpo, 2004). A better knowledge management of African traditional medicine procedures would improve their practice and the safety of their

[4] http://bioportal.bioontology.org/.
[5] http://www.w3.org/wiki/HCLSIG/AlternativeMedicineUseCase.
[6] http://www.lirmm.fr/cogui/.
[7] http://cogitant.sourceforge.net/.

patients. In this work, we have proposed a framework of formal requirements specification to improve traditional knowledge representation aiming at policy-making in order to detect flaws in the representation and to perform corrective actions.

We used conceptual graphs to visually express the formal requirements of compliance for procedural knowledge in the traditional medicine domain. Indeed, this formal specification provides the means to ensure more rigorous monitoring of compliance with the domain requirements, while allowing a better expression of the facts and an explanation of the stages of reasoning (Kamsu-Foguem et al., 2012). Each specification is associated with a temporal logic formula to enable the automated verification of compliance requirements models of domain knowledge. The information retrieval is formalised in a semantic similarity reasoning based on taxonomic knowledge. The mechanism consists in making sure that the logical formula associated to the local requirements specification of ATM subsumes the logical formula associated to the global medical specification applied for that particular case.

Our approach to visual representation of the reasoning steps with the graphs operations has two major advantages. First, analysts of medical practices can rigorously define compliance requirements without detailed knowledge of logical specification languages. Second, the visual character of the reasoning stages on the knowledge models, promotes understanding by domain analysts providing solutions for improving the quality of the modeled knowledge for reuse of best traditional medical practices for example (Kamsu-Foguem et al., in press). In order to overcome the drawbacks of CG models, we have introduced temporal CGs (i.e. a type of nested graphs) that are formally defined by a clear temporal semantics within the CTL-based framework. Being relied on CTL, temporal CGs capture adequately the semantics to enable formal specification of temporal properties of ATM domain knowledge, and so this improves the expressive power of CGs for knowledge modeling.

Some aspects of the management of traditional medical knowledge have not been taken into account in the present work and deserve to be investigated in the future prospects. For instance, it is worth investigating about the integration of requirements specified according to the principles of Good Laboratory Practices (chemical, pharmacological and toxicological evaluations) in order to check the bioactive properties of medicinal plants (WHO, 2009).

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