Contribution to the study of medicinal plants used in the treatment of diabetes, obesity and hypertension in Tafilalet region (Morocco)

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Abstract: The aims of the current review were to give an overview of the contribution of our research team to the study of antidiabetic, antihypertensive and anti-obesity medicinal plants in the southeastern region of Morocco (Tafilalet). A systematic literature search using PubMed, Scopus, and ResearchGate was conducted in regard to studies (established by our research team and those carried out by other researchers) that evaluated pharmacological interventions aiming to ameliorate diabetes mellitus, hypertension and obesity using medicinal plants, particularly investigations carried out within our laboratory. Since 2000 to nowadays, more than 37 pharmacological studies were carried out by our research team concerning axis previously cited. Furthermore, we reported in this review that among 90 plants cited in an enquiry conducted in Tafilalet region, 45 were pharmacologically studied by different researchers throughout the world. We present in this review the contribution of our team to the investigation of medicinal plants possessing potential pharmacological effects on diabetes mellitus, hypertension and obesity.

Keywords: diabetes, hypertension, obesity, Tafilalet, medicinal plants.

Introduction

Diabetes mellitus, cardiovascular, hypertension and obesity are four chronic pathologies responsible for a wide range of complications. In fact, several factors are involved in the appearance of these pathologies among large and different categories of people. The lifestyle changes, such as the restricted food which becoming more and more caloric and contaminated by toxic compounds as free radicals or pesticides, stress related to the life's constraints like those related to job and traffic, the effects of environmental changes characterized by the contamination of soil, air, water and food by various polluting agents are suspected to be involved in the pathogenesis of these diseases.

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Despite recent advances in the prevention and treatment of these disorders, people still prefer to use herbal medicines prescribed by local healers or recommended by a neighbor, a friend or a member of the family. Data furnished by the World Health Organization (WHO) indicate that over 80% of the worldwide population in rural areas has recourse to the alternative or traditional medicine to treat diverse illnesses in different health care systems. However, further experiments and studies are required to demonstrate effectiveness, safety and reliability of these herbal medicines.

Rich biodiversity provides to human a great garden of flora which should be exploited to prevent and remedy enormous and diverse health's problems. Great variation of climate and relief makes Morocco one of the richest countries floristically in the Mediterranean basin (Aaffi et al., 2002). Tafilalet, located at the south east of Morocco is considered as an interesting botanical area, it is characterized by richness and diversity of botanical species. In fact, an ethnobotanical survey carried out by our research team in 2002 demonstrated that local population of Tafilalet used largely the medicinal plants to care diabetes mellitus, hypertension and obesity (Eddouks *et al.*, 2002).

We aimed trough this review to summarize the research works carried out by our research team named Physiology and Endocrine Pharmacology (PEP). Our research team targeted since 2000 to carry out pharmacological and ethnopharmacological studies on medicinal plants used by local population of Tafilalet for the treatment of diabetes mellitus, hypertension and obesity.

Presentation of the area of study

Tafilalet (Errachidia province) is a province located at the south-east of Morocco between the latitudes 29°30' and 32°30' in the Drâa-Tafilalet region with a surface of 60 000 km^2. This province is limited on the north by the province of Midelt, in the northeast by the province of Figuig, in the South and southeast by Algeria and in the west by the two provinces of Zagora and Tinghir. According to the latest census (2014), the number of population in this province was 418 451 inhabitants, including more than 224 317 in rural areas. Tafilalet is the most important oasis of the Moroccan part of the Sahara Desert; it is also considered one of the largest oases in the world. The inhabitants of the oasis and region occupy fortified villages (Qsar). The climate is semi-arid. Rainfall is generally less to 100 mm/year and temperature oscillates between 8 °C (December-January) to 31.5 °C (July-August). Vascular flora of the areas of the southeast of Morocco (Tafilalet) is very surprising by its richness and the

diversity of its origin (Ozenda, 1958; Ozenda, 1991 and Bellakhdar, 1992). Despite its poor amount of precipitations, Tafilalet is characterized by a rich biodiversity which is translated in its interesting and fabulous vascular flora. The number of species arises to approximately 500, from which a big number is common or endemic at the semi-arid and Saharan areas (Ozenda, 1983).

Tafilalet is well marked by an interesting biodiversity, a rich history and ethnic diversity mixture of cultures, traditions and folklore making this region a natural source of traditional medicine. Particularly, this region is characterized by the richness of knowledge related to the traditional phytotherapy; this reflects the place of botanicals in the system health care within indigenous population.

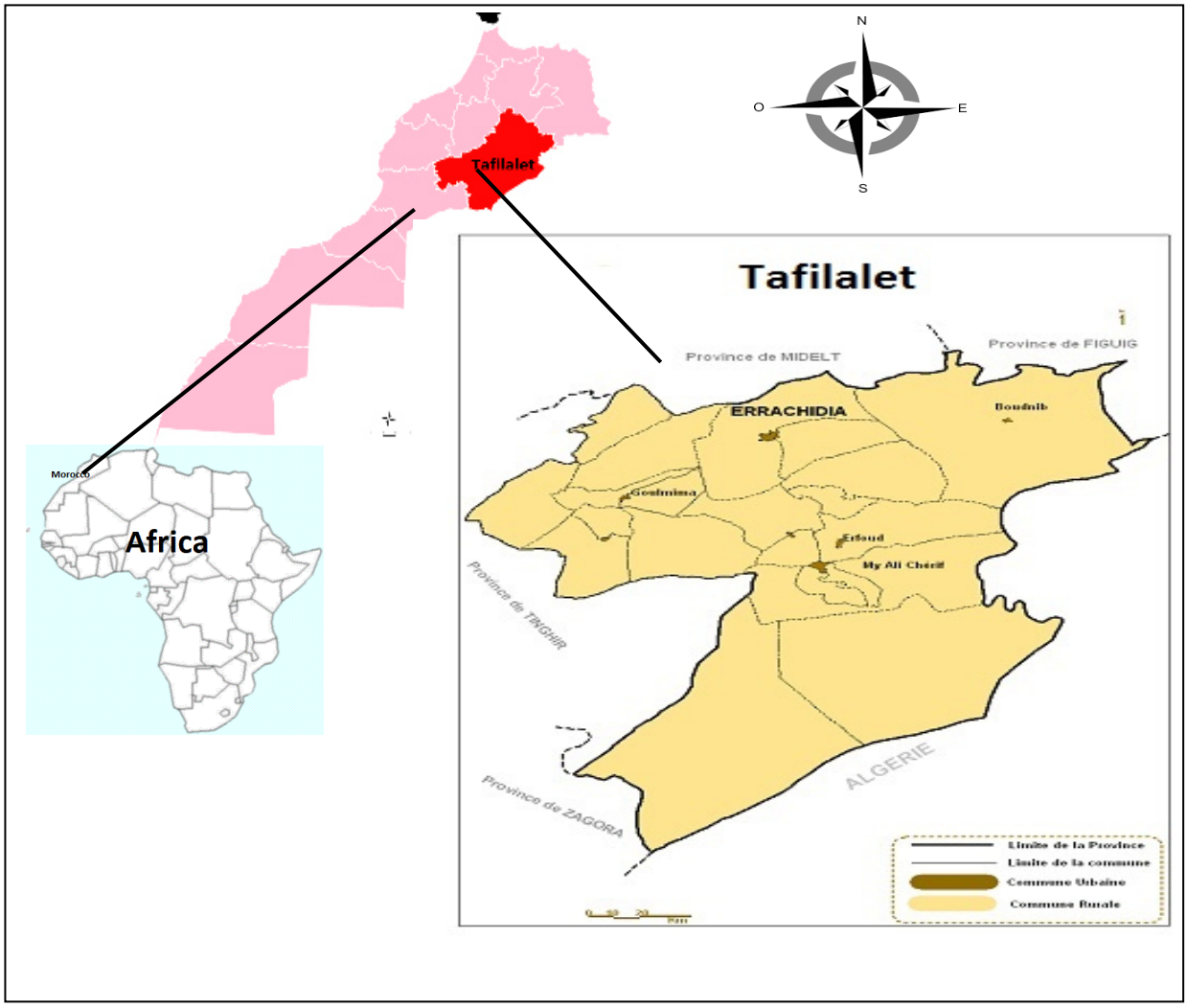

Figure 1: localization of the region of study (Tafilalet region).

Diabetes mellitus and hypertension in medicinal folk of Tafilalet

Our research team has carried out an ethnobotanical survey in Tafilalet region (Eddouks *et al*., 2002). The objective of this enquiry was to inventory medicinal herbs used by local population for the treatment of diabetes mellitus, hypertension and cardiac disorders. Six villages that belong to the area of study were interested by this investigation: Errachidia, Boudnib, Goulmima, Erfoud, Rissani and Rich. The sample size chosen for this enquiry was N=700. Among the 700 persons interviewed, 320 were diabetic patients and 380 patients with hypertension and cardiac disorders and 20 were herbal healers. Ninety-two medicinal plants were cited in this enquiry to be used as remedy for treating diabetes mellitus, hypertension and/or cardiovascular disorders. These species are distributed as following: 37 for treating diabetes mellitus, 73 for caring hypertension and cardiovascular disorders. A large number of species reported in this survey were never previously investigated (Table 1) (Eddouks *et al*., 2002). Several species were experimentally studied and supported by pharmacological investigations, either for their hypoglycemic effects or for their hypotensive and cardiovascular activities or for their anti-obesity activity by our research team (Table 2).

Table 1: medicinal plants quoted in the ethnopharmacological survey realized by our research team in 2002 and pharmacological (diabetes, hypertension and cardiac disorders) research works that were carried out on these plants.

Family and species names	Other areas of traditional use	Biological activity experimented			Part used	Comment about activity	Reference
		D	H	CD			
Apiaceae *Coriandrum sativum* L.	Middle East, Africa, Asia	✓	✓	✓	Seeds	• Extracts reduce blood glucose in alloxan-treated rats • Coriander fruit reveals gut stimulatory, inhibitory and hypotensive effects mediating possibly through cholinergic, Ca^{2+} antagonist and the combination of these mechanisms respectively • Methanolic extract of *Coriandrum sativum* prevent myocardial infarction by inhibiting myofibrillar damage, is also responsible for preventing oxidative damage	Sabu and Kuttan, 2003 Qaiser *et al.*, 2009 Dipak *et al.*, 2012
Apiaceae *Foeniculum vulgare* Mill.	Middle East	✓	✓			• Essential oil of *Foeniculum vulgare* Mill improve the hyperglycemia and pathological abnormalities in diabetic induced rats	Abou El-Soud *et al.*, 2011

				• Water extract of *Foeniculum vulgare* displayed a hypotensive effect in spontaneously hypertensive rats	El Bardai *et al*., 2001
Apiaceae *Heracleum sphondylium*	Europe	✓	Aerial parts	• Dichloromethane extract of *Heracleum sphondylium* L. exhibits vasorelaxant properties on rat isolated thoracic aortic rings	Senejoux *et al*., 2013
Apiaceae *Petroselinum sativum* Hoffm.	Middle East	✓	Fruits	• Diabetic rats treated with parsley showed significantly lower levels of blood glucose	Bolkent *et al*., 2004
Apiaceae *Pimpinella anisum* L.	Asia	✓	Seeds	• Methanolic extract and other fractions from aniseeds displayed anti-diabetic activities in terms of α- amylase and α-glucosidase inhibitory activities *in-vitro*	Shobha *et al*., 2013
Apocynaceae *Nerium oleander* L.		✓	✓ Flowers and leaves	• *Nerium oleander* improves glycaemia and contributes to treatment of type 2 diabetes by modulating cellular glucose uptake • Standardized hydromethanolic extract of *Nerium oleander* possess potent anti-diabetic activity in alloxan induced diabetic mice	Yazihan *et al*., 2013 Priyankar *et al*., 2015 Gayathri *et al*., 2010

				• Hydroethanolic extract of N oleander flower improves the antioxidant defensive role of myocardium	
Apocynaceae *Vinca minor* L	Africa, Europe, Middle East	✓ ✓	Whole plant	• Range of alkaloids including isoreserpiline and reserpiline have antidiabetic activity • Pharmacological studies of the total alkaloid sum of *Vinca minor,* have shown that when injected intravenously produces a continuous decrease of blood pressure in rats and rabbits	Marles and Farnsworth, 1995 Roussinov *et al*., 1962
Asteraceae *Matricaria camomilla*	Europe, Asia and N. Africa	✓ ✓	Flowers and whole plant	• Chamomile extract exhibited antidiabetic potential in alloxan-induced diabetic rats • Haemodynamic measurements were obtained prior to and 30 minutes after the oral ingestion of chamomile tea on 12 patients with cardiac disease who underwent cardiac catheterization	Estakhr and Javdan, 2011 Gould *et al*., 1973
Asteraceae *Inula viscosa* (Dryand.)	Middle East	✓	Leaves	• Extract lowers level of blood glucose • The aqueous extract obtained from *Inula viscosa* leaves prevented significantly the development of hypertension in L-NAME induced	Marles and Farnsworth, 1995

				hypertensive rats	
Asteraceae *Helianthus annuus* L	N. America	✓		Extract lowers blood glucose	Marles and Farnsworth, 1995
Asteraceae *Lactuca sativa* L.	Europe	✓	Leaves	Extracts lower blood glucose	Marles and Farnsworth, 1995
Berberidaceae *Berberis vulgaris* Vell.	India, Africa, Europe	✓ ✓	Roots, fruits	• Berberine administration to impaired glucose tolerance rats reduces levels of fasting blood glucose, triglycerides and total cholesterol • Hydro-ethanolic extract of *Berberis vulgaris* fruits has strong effect on heart contractility	Leng *et al*., 2004 Parsaee *et al*., 2006
Caryophyllaceae *Herniaria glabra* L.	N. Africa	✓		• Treatment with *H. glabra* saponins led to progressive decline in both systolic and diastolic blood pressures in Spontaneously hypertensive rats	Rhiouani *et al*., 2001
Chenopodiaceae				• Crude extract from leaves of	Mi-Jang *et al*., 2011
		✓			

Chenopodium ambrosioides L.	Asia	✓	Leaves	*Chenopodium ambrosioides* possess antidiabetic effect • Extracts from leaves of *C. ambrosioides*induce hypotensive effect on rats pretreated with L-NAME	Assaidi *et al*., 2014
Compositae *Artemisia absinthium* L.		✓	Aerial part, leaves	• Ethanol extract of *Artemisia absinthium* demonstrated a significant antihyper-glycemic effect on alloxan-induced diabetic rats	Haytham *et al*., 2014
Compositae *Helianthus annuus* L	India and N. Africa	✓	Seeds	• The methanolic extract from seeds of *Helianthus annuus* shows a potential antidiabetic property in Type 2 diabetes mellitus	Shivani and suni (2013)
Compositae *Lactuca scariola* L.	India and N. Africa	✓	Leaves	• *Lactuca scariola* leaves aqueous extract showed a significant glucose tolerance and hypoglycemic regulation of blood sugar in diabetic rats • Methanol extract of *Lactuca serriola* was found to possess vasorelaxant activity on Isolated Rabbit Aorta	Chadchan *et al*., 2015 Janbaz *et al*., 2013
Cucurbitaceae *Citrullus colocynthis*	Middle East and N. Africa	✓	Rind	• Aqueous extract of the rind of *C. colocynthis* possesses a hypoglycaemic in normal and alloxan-induced diabetic rabbits	Issa *et al*., 1999
Fabaceae	Asia, Europe	✓		• Water extract of the dried root,	Kim *et al*., 1990

Glycyrrhiza glabra	and Africa		Roots	administered intragastrically to mice after streptozotocin was effective	
Equisetaceae *Equisetum arvense* L.	Asia and N. Africa	✓	Whole plant	• Methanolic extract of *Equisetum arvense* showed a significant hypoglycaemic activity in streptozotocin induced diabetic rats	Soleimani *et al*., 2007
Globulariaceae *Globularia alypum* L.	N. Africa	✓ ✓	Leaves	• Infusion of *Globularia alypum* leaves produced a significant hypoglycaemic effect in normal and hyperglycaemic rats • Aqueous extract of *Globularia alypum* reduced metabolic disorders and oxidative stress induced in rats fed a high-fructose diet	Skima *et al*., 1999 Taleb-Dida, 2011
Graminae *Cynodon dactylon*	N. Africa an India	✓ ✓		• Aqueous extract of *Cynodon dactylon* has high antidiabetic potential in streptozotocin-induced diabetic rats • Administration of *C. dactylon* in monocrotaline-injected rats exerted a strong protective effect on right heart failure	Santosh *et al*., 2007 Alireza *et al*., 2009
Lamiaceae *Lavandula dentata* L.	Europe, Asia and Africa	✓	Leaves	• Infusions of *L. dentata* and *L. latifolia* exerted hypoglycemic effects in hyperglycemic and normoglycemic rats	Gamez *et al*., 1988

Lamiaceae *Marrubium vulgare* L.	Africa, Asia and Meedle East	✓ ✓	Aerial parts	• Methanolic extract of *Marrubium vulgare* significantly reduced the blood glucose level and increased in plasma insulin and tissue glycogen contents for streptozotocin-induced diabetic rats • Methanolic extract of *Marrubium vulgare* protects myocardium against isoproterenol-induced acute myocardial infraction	Elberry *et al*., 2011 Youssefi *et al*., 2013
Lamiaceae *Salvia officinalis*L.	Europe, Africa	✓	Leaves, aerial parts	• Extracts of *Salvia officinalis* decrease blood glucose level in alloxan-treated mice	Alarcon–Aguilar *et al*., 2002
Lamiaceae *Mentha spicata* L.	N. AfricaAmerica	✓	Leaves, aerial parts	• The offspring from diabetic dams treated with peppermint showed significantly reduced levels of glucose	Barbalho *et al*., 2011
Lamiaceae *Rosmarinus officinalis* L.	Africa and Europe	✓	Leaves, aerial parts	• Extract of *Rosmarinus officinalis* L. has an antihyperglycaemic effect that was accompanied by a significant increase in serum insulin levels in diabetic rabbits	Bakırel *et al*., 2008
Lamiaceae *Thymus vulgaris*		✓ ✓		• Supplementation with *T. vulgaris* as herbal remedy has revealed an important antihypertensive effect and	Kensara *et al*., 2013

	Africa and Europe		Aerial parts	manifested enhancement on hypertension-related biochemical changes and aortic vascular damage in rats	
Lauraceae *Cinamomum cassia*	Asia	✓ ✓	Bark	• Cinnamon acetone extract and Cinnamon water extract have a higher anti-hyperglycemic effect via inhibition of carbohydrate hydrolyzing enzymes • Administration 2-methocycinnamaldehyde, one of active ingredients of *Cinnamomum cassia* significantly improved I/R-induced myocardial dysfunction	Kang *et al*., 2014 Hwa et al., 2012
Leguminosae *Lupinus albus* L.(sensu Lato)	Africa and Meadle East	✓	Seeds	• *Lupinus albus* seed powder caused a profound hypoglycemic action in normal and diabetic rabbits	Helmi, 1969
Leguminosae *Trigonella foeniculum-graecum* L.	Africa and Meadle East	✓	Fruits	• Extract of significantly reduced glycemia in STZ-diabetic rats	Vats, 2003
Liliaceae *Allium cepa* L.	Africa, Asia and Meadle East	✓ ✓	Bulb	• Petroleum ether extract produced strong activity vs epinephrine and alloxan-induced hyperglycemia • Ethanol (70%) extract of the fresh bulb, administered intravenously to rats at variable dosage levels, was	Osman, 1980 Adesina, 1982

				active	
Liliaceae *Allium sativum* L.	N. Africa, Asia and Meadle East	✓	Bulb	• Extract of bulb of *Allium sativum* lowers blood sugar at a level comparable to tolbutamide stimulates insulin secretion from β-cells, improves glucose tolerance and increases liver glycogen synthesis	Li *et al*., 2004
Linaceae *Linum usitatissimum* L. (angustifolium Huds)	Africa and India	✓ ✓	Seeds	• Ethanolic extract of *L. usitatissimum* showed antihyperglycaemic effect via inhibition of ROS level in peripheral blood mononuclear cells, and preserves endogenous antioxidant enzymes in pancreatic tissue in alloxan-induced diabetic rats. • *Linum usitatissimum* possess a cardioprotective protective effect in isoprenalin-induced cardiotoxicity	Ghule *et al*., 2012 Zanwar *et al*., 2011
Loranthaceae *Viscum album* L.	Asia, Europe, India	✓	Aerial parts	• Extracts of this plant inhibit α-glucosidase	Onal *et al*., 2005
Lythraceae *Lawsonia inermis*	Africa	✓	Aerial parts	• Methanol (95 %) extract of leaves of *L. inermis* exhibited significant *in-vitro* antihyperglycemic effect	Arayne *et al*., 2007
Myrtaceae	Asia			• *Eugenia caryophyllata*-derived oleanolic acid (OA) had been reported	Ngubane *et al*., 2011

Eugenia caryophyllata	(Indonisia), America and Africa	✓	Cloves	to be mediated in part via increased hepatic glycogen synthesis in streptozotocin- induced diabetic rats	
Myrtaceae *Myrtus communis* L.	Africa	✓	Leaves and stem	• Extract of *Myrtus communis* reduces blood glucose	Ivorra *et al*., 1989
Oleaceae *Olea europaea* L.	Mediterannean region	✓	Leaves	• Extract of leaves contains luteolin and oleanolic acid, which are antihyperglycemic agents; oleanolic acid also inhibits α-amylase	Komaki *et al*., 2003
Pedaliaceae *Sesamum indicum* Dc.	Meedle East and India	✓	Seeds	• Hot water and methanol extracts fed to mice reduce blood glucose associated with a delay in glucose absorption	Takeuchi *et al*., 2001
Punicaceae *Punica granatum* L.	Africa, Europe and Asia	✓	Fruits and flowers	• Methanol seed extract reduces glucose levels in streptozotocin-inducted rats	Das *et al*., 2001
Rosaceae *Prunus amygdalus* stokes var. amara CD.	Africa, Asia	✓	Seeds	• *Prunus amygdalus* seeds were found to exert a significant hypoglycemic action on albino rabbits	Teotia and Sangh, 1996
Viticeae *Vitis vinifera*	Whole world	✓ ✓	Grape seeds and leaves	• Ethyl acetate fraction from leaves of *Vitis vinifera* had a significant antihyperglycaemic activity equipotent with the reference hypoglycaemic agent (tolbutamide) in diabetic rats • Oral consumption of standardized grape extract of *Vitis vinifera*	Orhan *et al*., 2006 Cui *et al*. , 2002

				provided significant cardioprotection by improving post-ischemic ventricular recovery and reducing the amount of myocardial infarction in rats	
Zygophyllaceae *Peganum harmala* L.	Central Asia, North Africa and Middle East	✓ ✓ ✓	Seeds	• Extracts from seeds of *Peganum harmala* have hypoglycemic activity • harmine, harmaline and harmalol are three alkaloids isolated from *Peganum harmala* with vasorelaxant effects • The same three isolated alkaloids isolated from *P. harmala* have ionotropic effect and decrease heart rate in normal anesthetized dogs	Marles and Farnsworth, 1995 Shi *et al*., 2001 Aarons *et al*., 1977
Zygophyllaceae *Zygophyllum gaetulum* Emb. Maire	Africa	✓	Whole plant	• Aqueous extract of *Zygophyllum album* decreases glucose blood level on streptozotocin-induced diabetic mice	El Ghoul *et al*., 2011

D: diabetes; **H**: hypertension; **CD**: cardiac disorders

In this ethnobotanical survey, 92 medicinal plants were quoted and identified (Eddouks *et al*., 2002). While, 45 (49%) were pharmacologically investigated and the activity has been traditionally recognized and confirmed worldwide (species studied in our laboratory are excluded from these species cited in table 1). Therefore, this important percentage (49%) demonstrates the validity and reliability of the information collected from this enquiry. In addition, some medicinal plants had additional pharmacological activities such as *Foeniculum vulgare* which was cited only for its antidiabetic traditional use, but pharmacological investigations revealed that this plant is efficient as an antihypertensive agent (El Bardai *et al*., 2001); *Matricaria camomilla* was cited in this survey as remedy for cardiovascular diseases, however, pharmacological investigations showed that this herb possess antidiabetic action also (Estakhr and Javdan, 2011); *Berberis vulgaris* and *Vitis vinifera* extracts improved glucose tolerance in diabetic rats (Leng *et al*., 2004; Orhan *et al*., 2006).

Literally, ethnobotanical surveys present a valuable source of information concerning traditional knowledge and have an extraordinary effect over experimental aspect of medicinal plants. In the same context, the majority of researchers dealing with the study of pharmacological effects of medicinal plants are based on findings obtained from this sort of investigations and they consider it as a rigid background. Moreover, several studies have confirmed that there is a significantly higher rate of pharmacological activity in plant extracts used ethnomedically compared to extracts from randomly collected plants (Iwu and wooton, 2002). In this context, several bioactive molecules of conventional drugs were isolated from medicinal plants that are currently used as remedies in traditional medicine of an indigenous population somewhere in the world; therefore, the isolation of the antimalarial drug, quinine, from the bark of *Cinchona* species (e.g. C.*officinalis)* was revealed in 1820 by two French pharmacists, Caventou and Pelletier, this natural compound formed the basis for the synthesis of the commonly used antimalarial drugs, chloroquine and mefloquine. The bark of this herb

had long been used by indigenous groups in the Amazon region for the treatment of fevers before being introduced into Europe in the early 1600s in order to treat malaria. Another plant long used as remedy against fevers in traditional Chinese medicine, *Artemisia annua*, has produced the agents, artemisinin and its derivatives, artemether and artether, that are revealed to be effective against resistant strains (Gokhale et al.,1999). Other significant drugs developed from traditional medicinal plants.

Contribution of our laboratory to the study of antihyperglycemic, antihypertensive and anti-obesity plants

Our research investigations were based on the ethnobotanical survey cited above. In fact, ethnobotanical enquires constitute a precious library for pharmacological studies because information and data concerning traditional medicine collected from a given indigenous people in this type of studies are very rich and are often reliable when are carried out correctly. Furthermore, the set of this information constitutes a heritage from our ancestors, which accumulated a big knowledge from generation to generation, and traditional medicines can be a major source of novel medicines. According to Iwu and wooton, (2002), the wealth of ethnomedical information on its efficacious use in the long history of traditional medicine is a major factor that contributes to select one or more medicinal plant candidates for development into phytomedicines (Iwu and wooton, 2002). Medicinal plants or their extracts have been used by humans since time immemorial for different ailments and have provided valuable drugs such as analgesics (morphine), antitussives (codeine), antihypertensives (reserpine), cardiotonics (digoxin), antineoplastics (vinblastine and taxol) and antimalarials (quinine and artemisinin) (Ramawat *et al*., 2009). All the previous factors and others push pharmacologists to base on results obtained from ethnobotanical surveys.

Our pharmacological studies were performed on laboratory animal models and were based on three main axes: antidiabetic activity, cardiovascular and antihypertensive investigation and anti-obesity pharmacological activity. All these investigations realized from

2000 to nowadays are summarized in table 2. Our objective was to investigate medicinal plants and preparations used locally by population and traditional healers in Tafilalet for treating diabetes mellitus, hypertension and cardiac disorders taking into consideration local mode of preparations and doses recommended by traditional practicing or patients. All these are summarized in table 2.

Table 2: summarize of the research carried out in the PEP laboratory between 2000 and 2016.

Activity	Plant species	Vernacular name	Date of study	Part used	Dose (mg/kg)	Animal model Used	Reference
Antidiabetic activity	Caryophyllaceae *Spergularia purpurea* (Pers.) G.Don	زهرة الرمال	2000	Whole plant	10	Wistar rats strepto-zotocin (STZ)	Jouad *et al*., 2000
	Chenopodiaceae *Suaeda fruticosa*		2001	Whole plant	192	Wistar rats (STZ)	Benwahhoud *et al*., 2001
	Rosaceae *Rubus fructicosus* L.	التوت الشوكي	2002	Leaves	100	Wistar rats (STZ)	Jouad *et al*., 2002a
	Plantaginaceae *Globularia alypum*	عين الارنب	2002	Leaves	20	Wistar rats (STZ)	Jouad *et al*., 2002a
	Apiaceae *Ammi visnaga*	البشنيخة	2002	Fruits	20	Wistar rats (STZ)	Jouad *et al*., 2002b
	Rosaceae *Crataegus oxyacantha*	أدمام	2003	Leaves	150 and 300	Wistar rats (STZ)	Jouad *et al*., 2003a
	Caryophyllaceae *Spergularia purpurea* (Pers.) G.Don	زهرة الرمال	2003	Aerial part	10	Mice	Eddouks *et al*., 2003

						(STZ)	
	Myrtaceae *Eucalyptus globulus*	كاليبتوس	2003	Leaves	150 and 300	Wistar rats (STZ)	Jouad *et al*., 2003b
	Fabaceae *Retama raetam* Forssk	الرطم	2003	Leaves	20	Wistar rats (STZ)	Maghrani *et al*., 2003a
	Lamiaceae *Calamintha officinalis* Moench	مانتة	2004	Aerial part	20	Wistar rats (STZ)	Lemhadri *et al*., 2004a
	Oleaceae *Fraxinus excelsior* L.	لسان العصفور	2004	Aerial plant	10	Wistar rats (STZ)	Eddouks and Maghrani, 2004
	Lamiaceae *Origanum vulgare*	الزعتر	2004	Leaves	20	Wistar rats (STZ)	Lemhadri *et al*., 2004b
	Apiaceae *Carum carvi*	الكروية	2004	Fruits	20	Wistar rats (STZ)	Eddouks *et al*., 2004a
	Capparidaceae *Capparis spinosa* L.	الكبار	2004	Fruits	20	Wistar rats (STZ)	Eddouks *et al*., 2004a
	Oleaceae *Fraxinus excelsior* L.	لسان العصفور	2004	Aerial plant	10	Wistar rats (STZ)	Eddouks *et al*., 2004b
	Asteraceae *Silybum marianum*	شوك الجمال	2004	Seeds	20	Wistar rats (STZ)	Maghrani *et al*., 2004
	Asteraceae *Chamaemelum nobile* (L.) All.	البابونج	2004	Aerial part	20	Wistar rats (STZ)	Eddouks *et al*., 2004c
	Poaceae *Triticum repens* P. Beauv.	النجم البوري	2005	Rhizomes	20	Wistar rats (STZ)	Eddouks *et al*., 2005a
	Brassicaceae *Lepidium sativum* L.	حب رشاد	2005	Seeds	20	Wistar rats	Eddouks *et al*., 2005b

						(STZ)	
	Brassicaceae *Lepidium sativum* L.	حب رشاد	2008	Seeds	10	Wistar rats (STZ)	Eddouks *et al*., 2008
Antihypertensive activity	Caryophyllaceae *Spergularia purpurea* (Pers.) G.Don	زهرة الرمال	2001	Whole plant	100, 200 and 400	Wistar rats	Jouad *et al*., 2001a
	Caryophyllaceae *Spergularia purpurea* (Pers.) G.Don	زهرة الرمال	2001	Whole plant	5 (flavonoids mixture)	Wistar rats	Jouad *et al*., 2001b
	Oleaceae *Fraxinus excelsior* L.	لسان العصفور	2005	Seeds	20	Wistar rats	Eddouks *et al*., 2005c
	Fabaceae *Retama raetam* Forssk	الرطم	2007	Leaves	20	Wistar rats	Eddouks *et al*., 2007
	Brassicaceae *Lepidium sativum* L.	حب رشاد	2005	Seeds	20	Wistar rats	Maghrani *et al*., 2005a
	Fabaceae *Retama raetam* Forssk	الرطم	2005	Seeds	5	Wistar rats	Maghrani *et al*., 2005b
	Asteraceae *Chamaemelum nobile* (L.) All.	البابونج	2008	Aerial parts	50, 100 and 140	Wistar rats	Zeggwagh *et al*., 2008a
	Asteraceae *Artemisia herba alba*	الشيح	2014	Aerial parts	50, 100 and 200	Wistar rats	Zeggwagh *et al*., 2014
	Asteraceae *Chamaemelum nobile* (L.) All.	البابونج	2016	Aerial parts	50, 100 and 200	In vitro	Hebi *et al*., 2016b
Cardiovascular activity	Asteraceae *Artemisia herb-alba* Asso	الشيح	2008	Aerial parts	150	Wistar rats	Zeggwagh *et al*., 2008b
	Asteraceae *Chamaemelum nobile* (L.) All.	البابونج	2013	Aerial parts	5, 10 and 20	Wistar rats	Zeggwagh *et al*., 2013
	Ranunculaceae *Nigella sativa* L.	الحبة السودة	2016	Seeds	50, 100 and	Rats and in	Hebi *et al*.,

					200	vivo	2016b
Anti-obesity activity	Caryophyllaceae *Spergularia purpure a*(Pers.) G.Don	زهرة الرمال	2003	Whole plant	10	Wistar rats	Jouad *et al*., 2003c
	Poaceae *Triticum repens* P. Beauv.	النجم البوري	2003	Rhizome	20	Wistar rats	Maghrani *et al*., 2003b
	Fabaceae *Retama raetam*	الرطم	2003	Whole plant	20	Wistar rats	Maghrani *et al*., 2003c
	Capparidaceae *Capparis spinosa* L.	الكبار	2005	Fruits	20	Wistar rats	Eddouks *et al*., 2005d
	Apiaceae *Carum carvi*	الكروية	2006	Fruits	20	Wistar rats	Lamhadri *et al*., 2006

PEP: Physiology and Endocrine Pharmacology

Antidiabetic activity

Diabetes mellitus (DM) is a chronic disorder characterized by hyperglycemia with disturbances of carbohydrate, fat, and protein metabolism resulting from defects in insulin secretion, insulin action, or both (King, 1999). Latest predictions submit that in the year 2025 more than 400 million people will have overt diabetes, mainly type 2 diabetes mellitus (T2DM), with excessive growth in developing countries (King *et al*., 1998). Several plants species possess bioactive molecules that have pharmacological effect against DM, and are historically used by human to care this endocrine disorder. Hypoglycemic natural products include flavonoids, xanthones, triterpenoids, glycosides, alkyldisulfides, aminobutyric acid derivatives, guanidine, polysaccharides, and peptides (Wang and Ng, 1999).

Table 2 illustrated the species studied by our research team since 2000 until 2016. Our research team carried out 20 pharmacological investigation concerning antidiabetic activities. Where, 17 medicinal plants were exploited for this purpose. Set of these species are treated below.

- *Spergularia purpurea*: the hypoglycaemic effect of this plant was investigated in normal and streptozotocin-induced diabetic (STZ) rats at a dose of 10 mg/kg. The extract showed a significant decrease in normal and diabetic streptozotocin-induced diabetic rats after 6 hours of treatment (single oral administration). While, for repeated oral administration (2 weeks of treatment) blood glucose levels were decreased after 4

days of treatment for diabetic rats and after 7 days of treatment for normal treated rats (Jouad *et al*., 2000). In the same context, and in order to determine the underlying mechanism of the hypoglycemic activity of the aqueous extract of this plant, another study was conducted in 2003 based on the infusion (intravenous administration) of the aqueous extract of this plant in diabetic mice and streptozotocin-induced diabetic rats. This study demonstrated that infusion of this extract inhibited endogenous glucose production in mice (Eddouks *et al*., 2003).

- *Suaeda fruticosa*: The purpose of this study was to examine the hypoglycemic activity of the aqueous extract of the aerial part of *Suaeda fruticosa* in normal and streptozotocin-induced diabetic rats. For this purpose, the aqueous extract (at a dose of 192 mg/kg) was administered intravenously in streptozotocin-induced diabetic rats. The results showed a significant decrease in blood glucose levels in normal rats, and even more in diabetic rats (Benwahhoud *et al*., 2001).

- *Rubus fructicosis* and *Globularia alypum*: The aqueous extracts of the two species were studied in order to demonstrate their hypoglycaemic effect. In normal rats, single and repeated oral administration of *Rubus fructicosis* (RF) lowered significantly the blood glucose levels, while, *Globularia alypum* (GA) treatment did not change blood glucose levels. In STZ rats, single and repeated oral administration of both RF and GA produced significant decrease of blood glucose levels. Furthermore, an acute toxicity study showed that the two extracts are relatively safe (Jouad *et al*., 2002a).

- *Ammi visnaga*: the aim of this study was to test the effect of the aqueous extract of fruits of *Ammi visnaga* on blood glucose levels in fasting normal and STZ rats after single and repeated oral administration as well as its acute toxicity (LD_{50}). Results of this study demonstrated a potential hypoglycemic effect in both normal and STZ rats and any deaths or major signs of acute toxicity were observed for the doses lower than 6.5 and 2.7 g/kg for oral and intraperitoneal administration respectively (Jouad *et al*., 2002b). In another pharmacological investigation realized by Rauwald et al (1994), two compounds were identified; visammin, which causes a relaxation of visceral plain muscle and khellinin, which dilates the coronary blood vessels in perfused rabbit's heart.

- *Crataegus oxyacantha*: in this pharmacological investigation, the aqueous extract from leaves of *C. oxyacantha* was tested in normal and diabetic rats; an acute toxicity

(LD_{50}) of the same extract was also carried out. The plant extract activity showed a significant decrease on blood glucose level for STZ rats, but no effect was observed in normal rats after a single dose or 9 daily doses (150 and 300 mg/kg). While, results obtained for acute toxicity test showed that the aqueous extract had a high LD50 value (13.5 g/kg) in mice (Jouad *et al*., 2003a). This species showed also in another investigation its ability to regulate both low and high blood pressure (Wagner *et al*., 1982). Glycoside component of this plant revealed increases vagal tone of the heart (Petkov *et al*., 1981).

- *Eucalyptus globulus*: in this study, both single and repeated oral administration of the aqueous extract of *Eucalyptus globulus* leaves at the doses of 150 and 300 mg/kg body weight displayed a significant hypoglycemic effect in streptozotocin diabetic rats. A test of oral acute toxicity study in mice demonstrated that the LD_{50} value for the *Eucalyptus globulus* leaf tissue was 4.5 g/kg (Jouad *et al*., 2003b). A pharmacological investigation which had the purpose to reveal the cardiovascular activity of the same plant, realized by Aswal et al (1984), exhibited that the Ethanol (50%) extract of the dried aerial part, administered intravenously to dogs was active.

- *Retama raetam*: the aqueous extract of leaves of this plant was tested for its antidiabetic effect in fasting normal and STZ rats after single and repeated oral administration of this extract at a dose of 20 mg/kg. The study demonstrated a potential hypoglycemic effect of this plant in normal and STZ rats (Maghrani *et al*., 2003a).

- *Triticum repens*: in this study, aqueous extract of rhizomes of this plant was tested in normal and STZ rats. Significant reduction on blood glucose levels were noted in diabetic and normal rats at a dose of 20 mg/kg (Eddouks *et al*., 2005a).

- *Calamintha officinalis*: water extract from the aerial parts of this herb was tested for plasma blood glucose concentrations and basal insulin levels in normal and STZ diabetic rats at a dose of 20 mg/kg. The results visibly demonstrated the hypoglycaemic effect of this plant extract in both normal and STZ diabetic rats after either a single dose or daily oral administration for 15 days. Whereas, basal plasma insulin concentrations were not affected (Lemhadri *et al*., 2004a).

- *Origanum vulgare*: The effect of an aqueous extract of leaves of this medicinal plant on blood glucose levels was investigated in normal and STZ diabetic rats. This extract

had a significant decrease of blood glucose levels in normal and STZ diabetic rats at a dose of 20 mg/kg (Lemhadri *et al*., 2004b).

- *Carum carvi*: The hypoglycaemic effect of aqueous extracts of fruits of *Carum carvi* at a dose of 20 mg/kg was investigated in normal and STZ diabetic rats. Results demonstrated a significant decrease on blood glucose levels in STZ diabetic rats after acute (6 hours) and chronic (14 days) treatment. While, no changes were observed on normal rats (Eddouks *et al*., 2004a).

- *Capparis spinosa*: In this study, the hypoglycaemic effect of aqueous extracts of fruits of *C. spinosa* (20 mg/kg) has been investigated. Results, showed a significant efficiency of this extract on STZ diabetic rats. Whereas, no effect was observed for normal rats (Eddouks *et al*., 2004a).

- *Fraxinus excelsior*: The hypoglycaemic effect of the aqueous extracts (20 mg/kg) of *Fraxinus excelsior* seeds was investigated in normal and STZ diabetic rats. After a single dose or 15 daily doses, oral administration of the aqueous extracts provoked a significant decrease of blood glucose levels in both normal and STZ diabetic rats. No changes were observed in basal plasma insulin concentrations in either normal or STZ diabetic rats (Eddouks *et al*., 2004b). Another study that aimed to determine the underlying mechanism of the hypoglycaemic activity of the same extract perfusion of this plant in normal and STZ diabetic rats. The results showed a potent inhibition of renal glucose reabsorption (Eddouks and Maghrani, 2004).

- *Silybum marianum*: aqueous extracts of *S. marianum* seeds have been studied for his antidiabetic activity. We concluded from this investigation that the aqueous extracts of this plant exhibited potent hypoglycaemic and anti-hyperglycaemic activities in normal and STZ rats (Maghrani *et al*., 2004).

- *Chamaemelum nobile*: we aimed trough this investigation to test the effect of both a single dose and daily oral administration for 15 days of the aqueous extract of the aerial part of *Chamaemelum nobile* at a dose of 20 mg/kg on blood glucose concentrations and basal insulin levels in normal and STZ diabetic rats. This study demonstrated that this extract exhibits a significant hypoglycaemic effect in normal and STZ diabetic rats without affecting basal plasma insulin concentrations (Eddouks *et al*., 2004c).

- *Lepidium sativum* L.: the purpose of this study was to confirm the use as a hypoglycaemic agent of *L. sativum* in traditional medicine. The aqueous extract of seeds of this plant was investigated in normal and STZ diabetic rats. The aqueous extract (20 mg/kg) produced a significant decrease on blood glucose levels in both STZ diabetic and normal rats after acute (6 hours) and chronic oral treatment (15 days). While, no changes were observed in basal plasma insulin concentrations after treatment either in normal or STZ diabetic rats (Eddouks *et al*., 2005b). This last study was supported by another work that aimed to determine the mechanism underlying the hypoglycaemic activity of the aqueous extract perfusion of *Lepidium sativum* L. in normal and STZ diabetic rats. This investigation was based on the intravenous administration of the extract and the blood glucose levels were determined within 4 h of treatment. Plasma insulin concentrations and glycosuria were determined. The 24 h urinary transforming growth factor-β1 was evaluated in diabetic and control rats 15 days after oral treatment with this extract at a dose of 20 mg/kg. The results demonstrated that this aqueous extract produced a potent inhibition of renal glucose reabsorption, which consequently reduced blood sugar (Eddouks *et al*., 2008).

Antihypertensive investigation

Systemic arterial hypertension is the state of persistent, non-physiologic elevation of systemic blood pressure (BP). At present, hypertension is defined as a resting systolic BP (SBP) ≥140 mm Hg or diastolic BP (DBP) ≥90 mm Hg (Chobanian *et al*, 2003). Many herbal preparations and plant species are used in certain health care systems and pharmacopeias to remedy problems related to blood pressure as hypertension. An herbal remedy that has been used in the treatment of mild to moderate hypertension is the whole extract made from the dried roots of Indian snakeroot (*Rauwolfia serpentina*), an evergreen shrub native to tropical Asia. The extract contains more than 50 different alkaloids, including the sympatholytic agent reserpine. Reserpine is one of the oldest antihypertensive agents and one of the most economical hypotensive agents (Jakob, *et al*, 1991).

Our team has contributed to the study of the antihypertensive plants and this contribution is summarized as follows:

- *Fraxinus excelsior* L.: the purpose of the investigation was to investigate the hypotensive effect of the aqueous extract of *F. excelsior* in both normotensive (WKY)

and spontaneously hypertensive rats (SHR). Results of this study demonstrated that aqueous extract of this plant exhibited hypotensive and diuretic actions. In fact, after 3 weeks of treatment this extract produced a significant decrease in systolic blood pressure in both SHR and WKY rats. Furthermore, the extract significantly enhanced the urination in both SHR and WKY (Eddouks *et al*., 2005c).

- *Retama raetam* Forssk: we aimed trough this investigation to assess the hypotensive and diuretic effect of the aqueous extract of *R. raetam*. For this reason, the aqueous extract (20 mg/kg) was orally administrated during three weeks for both normotensive (WKY) and spontaneously hypertensive rats (SHR). The aqueous *R. raetam* extract significantly decreased blood pressure and enhanced the diuresis via the increase on urinary potassium elimination without affecting sodium and chloride excretion in WKY rats. Furthermore, this extract produced a significant increase on urinary excretion of sodium, potassium and chlorides in SHR rats (Eddouks *et al*., 2007). In another study based in the examination of the acute diuretic of the aqueous extract of the same plant at a dose of 5 mg/kg/h in normal rats, this extract exhibited a significant diuretic effect (Maghrani *et al*., 2005b).

- *Spergularia purpurea* (Pers.) G.Don: this investigation aimed to evaluate the effects of flavonoids extracted from *Spergularia purpurea* on arterial blood pressure and renal function in normal and hypertensive in normotensive (WKY) and spontaneously hypertensive rats (SHR) rats. In SHR rats, daily oral administration of the flavonoid mixture (5 mg /kg for 1 week) displayed a significant decrease in blood pressure; indeed, it enhanced significantly the water excretion in the same rats. While, in WKY rats the same flavonoids exhibited blood pressure and increased significantly the urinary electrolytes elimination (Jouad *et al*., 2001). In order to support the hypotensive effect of the last plant, another investigation was carried out in 2001 to evaluate the diuretic effect of the *S. purpurea*. This investigation showed that the water extract of this plant at different the doses of 100, 200 and 400 mg/kg produced a significant and dose-dependent diuresis and increase in electrolytes excretion in normal rats after daily oral administration of the water extract tested for 4 weeks (Jouad *et al*., 2001b).

- *Lepidium sativum* L.: the antihypertensive and diuretic effects of the aqueous extract of *Lepidium sativum* were studied in both normotensive (WKY) and spontaneously hypertensive rats (SHR) at a daily oral dose of 20 mg/kg for 3 weeks. For SHR rats,

the study showed a significant decrease in arterial blood pressure, but no statistically significant change was observed in the same rats concerning the water excretion. While in WKY rats, no significant change was noted during the period of treatment concerning the arterial blood pressure; but the extract enhanced significantly the water excretion for this group of rats. A significant increase of urinary excretion of sodium, potassium and chlorides was noted in both SHR and WKY rats (Maghrani *et al*., 2005a).

- *Chamaemelum nobile*: this study aimed to evaluate the hypotensive activity of the aqueous extract of *Chamaemelum nobile* in spontaneously hypertensive rats (SHR) at a dose of 140 mg/kg. The results demonstrated the hypotensive and the diuretic effects of this extract after a single oral administration (24h) and a daily oral administration (3 weeks) (Zeggwagh *et al*., 2008a). In order to determine the underlying mechanism of action of water extract of *Chamaemelum nobile* involved in hypotensive activity, lyophilized aqueous extract was administered in the jugular vein, arterial blood pressure and heart rate were measured in the carotide artery over 120 min of injection throughout an invasive direct blood pressure measuring procedure. The study concluded that this extract exhibited a hypotensive effect that may be probably due to an alpha-adrenergic receptor blockade mechanism (Hebi *et al*., 2016a).

- *Artemisia herba-alba* Asso: we aimed trough this study to evaluate the cardiovascular and renal function after intravenous injection of *A. herba-alba* aqueous extract at the different doses of 50, 100 and 200 mg/kg in normal rats. According to the results of this study, the aqueous *A. herba-alba* extract possesses a potent acute hypotensive effect on normal rats. Furthermore, the extract perfusion may affect renal function to increase urine and electrolytes excretion (Zeggwagh *et al*., 2014).

Cardiac disorders and pharmacological studies

Heart disease, also known as cardiovascular disease, refers to diseases of the blood vessels and heart. Cardiovascular disease (CVD) has remained the leading cause of death worldwide despite the tremendous progress made in medical and surgical treatment for this disease (Kewal., 2011). While extensive research has made numerous treatments for CVD, there has been limited success in preventing or curtailing the progression of related pathological conditions. Therefore, development of preventive measures that can limit the

progression of pathological conditions is necessary to lower the incidence of morbidity and mortality. As a result, there is a strong interest in determining the role of food-based bioactive compounds in reducing the risk of CVD (Batchu *et al*., 2012). In the same context, our research team has contributed actively to this topic. All our works concerning cardiovascular pharmacological investigations are presented below according to the species plants studied:

- *Artemisia herba-alba* Asso: in this study, the cardiovascular effect of the aqueous extract of A. *herba-alba* was evaluated in spontaneously hypertensive rats. We concluded from this investigation that the aqueous extract of A. *herba-alba* possess an antihypertensive activity (Zeggwagh *et al*., 2008b).
- *Chamaemelum nobile*: the purpose of this study was to evaluate the *in vitro* vasorelaxant effect of *C. nobile* aqueous extract. Aortic ring isolated from Wistar rats and aqueous *C. nobile* extract at doses of 5, 10 and 20 mg/ml were used. Incubation of aqueous C. *nobile* extract for 30 minutes produced a significant shift of the dose–response curve to norepinephrine (NE). This study showed that aqueous C. *nobile* extract possesses *in vitro* vasorelaxant effect (Zeggwagh *et al*., 2013).
- *Nigella sativa*: in this study the cardiovascular effect of *Nigella sativa* was evaluated and the aqueous extract of this plant at the doses of 50, 100 and 200 mg/kg produced a dose dependent reduction in the mean arterial blood pressure accompanied by a significant fall in heart rate. In the same context, an *in vitro* experiment showed that incubation of the aqueous extract during 30 min caused a right shift of the contraction response curve of aortic ring to NE with a reduction of the maximal contraction response (Hebi *et al*., 2016b).

Obesity and overweight problems pharmacological activities

According to the World Health Organization, Obesity is an excess of body fat accumulation with multiple organ-specific pathological consequences. In 2014, more than 1.9 billion adults, 18 years and older, were overweight and over 600 million were obese (WHO, 2014). Obesity is well known to be responsible of a range of serious chronic disease, as for example hypertension, diabetes, dyslipidemia, heart failure, etc. (Naveed and Mike, 2009). Four species which are traditionally known in Morocco to possess anti-obesity effect were investigated in our laboratory and are discussed below:

- *Spergularia purpurea*: we aimed trough this investigation to evaluate the lipid-lowering activity of the aqueous extract of *Spergularia purpurea* (SP) in both normal and diabetic rats. A single (6h) and repeated (2 weeks) oral administration of the aqueous extract of SP at a dose of 10 mg/kg were tested in normal and STZ diabetic rats. Results of this investigation concluded that this extract caused a significant decrease in cholesterol and triglyceride plasma levels in both normal and STZ diabetic rats after 2 weeks of treatment (Jouad *et al*., 2003c).

- *Carum carvi*: the purpose of this study was to determine the effect of the aqueous extract of *carum carvi* at a dose of 20 mg/kg on the lipid metabolism in normal and STZ diabetic rats. The results showed that the aqueous extract of *Carum carvi* exhibited lipid and body weight lowering activities in severe hyperglycaemic rats after repeated oral administration of this extract (Lemhadri *et al*., 2006).

- *Triticum repens*: the investigation aimed to assess the lipid metabolism effect of the aqueous rhizomes extract (20 mg/kg) of *Triticum repens* (TR) in normal and recent-onset diabetic rats and plasma triglycerides, cholesterol concentrations were determined. After 2 weeks of treatment, the aqueous extract of TR exhibited lipid and body weight lowering activities in severe hyperglycaemic rats after repeated oral administration of this extract (Maghrani *et al*., 2003b).

- *Capparis spinosa*: the objective of this study was to examine the effect of single and repeated oral administrations of the aqueous extract of *Capparis spinosa* L. (CS) at a dose of 20 mg/kg on lipid metabolism in normal and STZ diabetic rats. This study concluded that the aqueous extract of CS (20 mg/kg) exhibited a potent lipid lowering activity in both normal and severe hyperglycemic rats after repeated oral administration of CS aqueous extract (Eddouks *et al*., 2005d).

- *Retama raetam*: the aqueous extract of *Retama raetam* (RR) at a dose of 20 mg/kg was tested in normal. The results showed that this extract possess lipid and body weight lowering activities in both normal and severe hyperglycemic rats after repeated oral administration of RR aqueous extract at a dose of 20 mg/kg (Maghrani *et al*., 2003c).

The number of research studies that were carried out by our research team between 2000 and 2016 and that targeted the four previous pathologies (Diabetes, hypertension, cardiovascular problems and obesity) was fixed in 37 studies leading to the publication of more than 70 international papers. Where, 23% of works were realized in 2003 and 20% were

carried out in 2004. Concerning the rate of each category of pharmacological studies, 54% of the total of these studies were focalized on DM, 24% for hypertension, 13% for obesity and 8% for cardiovascular field.

Spergularia purpurea, a medicinal plant belonging to the family Caryophyllaceae, is the species the most studied in our laboratory with four studies where two studies were carried out for its antidiabetic effect, one for its hypotensive potent and one other for its lipid-lowering activity. *Chamaemelum nobile* was studied one time for its antidiabetic effect, two times for its hypotensive power and one time for its cardiovascular activity. While, species such as *Lepidium sativum* or *Capparis spinosa* were targeted for three and two investigations respectively. This undoubtedly confirms the pharmacological and therapeutic efficiency of these medicinal plants used in medicinal folk in Morocco. Thirteen botanical families were studied in our laboratory since 2000 to 2016 where Asteraceae is the botanical family the most common and targeted in our research investigations (Figure 2), species belonging to this family were particularly related to cardiovascular and antihypertensive pharmacological activities. While, Caryophyllaceae occupy the second place in list of families studied pharmacologically by our research team in DM, Hypertension and Obesity.

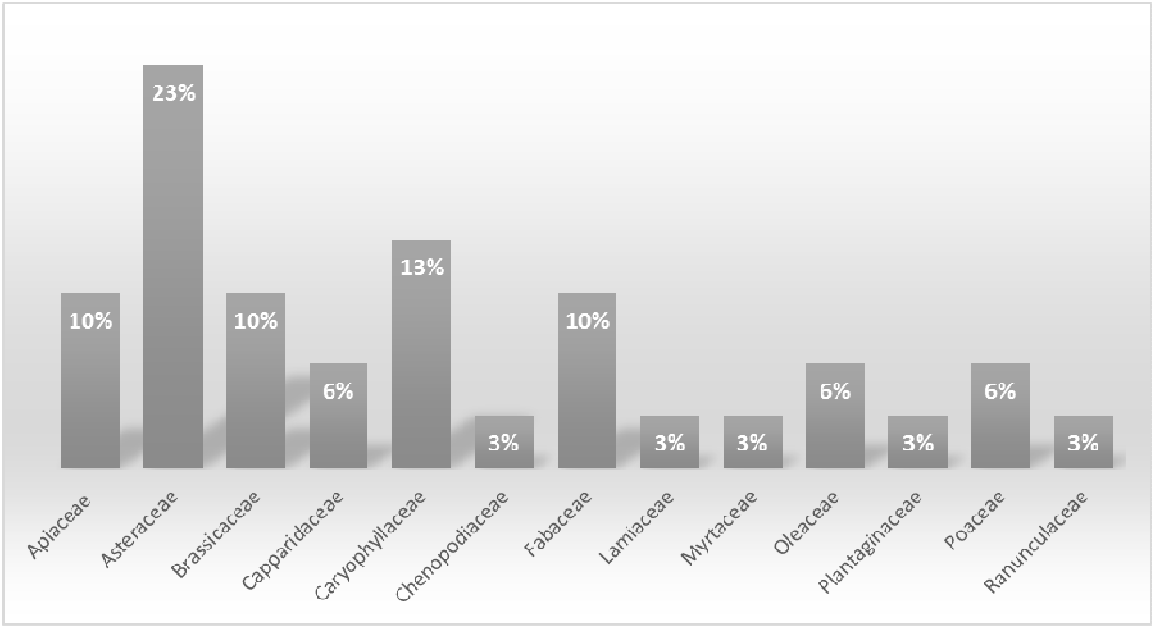

Figure 1: percentages of botanical families used for pharmacological studies by PENP team between 2000 and 2016.

In fact, our research team adapts a flexible strategy that aims in same time to diversify the plants and fields of research, this in order to highlight the natural sources (especially of medicinal plants of Tafilalet region) that possess potential pharmacological effects, and to advance our knowledge on medicinal plants. Additional logistic means and collaborative strategy are still necessary to elucidate the molecular mechanisms of active medicinal plants and to isolate bioactive molecules responsible for the biological and pharmacological effects of these plants.

Conclusion

Our research team has contributed actively to the study of the Moroccan pharmacopeia during the last 16 years and more than 20 plants from Moroccan medicinal plants have been demonstrated to have a beneficial effect on diabetes, hypertension and obesity and might be potential candidates for novel drugs developments. Despite the diversity and importance of research works that were carried out by our research team, several other efforts are needed to perform comprehensive studies of the mechanisms of action, the phytochemical and toxicological studies related to these medicinal plants.

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