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Some popular medicinal plants and diseases of the Upper Palaeolithic in Western Georgia

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ABSTRACT

Ethnopharmacological relevance: Palynological studies of cultural layers of cave sediments have been used in order to better understand traditional practices. The Upper Palaeolithic in Georgia (36,000 – 11,000 cal. BP) provides a rich source of such material. However, up to day from such sediments the identification of medicinal plants has hardly been achieved. Large quantities of pollen most notably from entomophilous taxa in fossil spectra can serve as a tool to identify traditionally important species. As these plants are used in modern popular medicine on the territory of Georgia (like *Achillea millefolium* L., *Artemisia annua* L., *Artemisia absinthium* L., *Centaurea jacea* L., *Urtica dioica* L.) can be served as an indirect evidence for their medicinal relevance from the Palaeolithic Period up to days. Their modern uses may point that the main diseases during the Upper Palaeolithic were the same as today.

Materials and methods: The Upper Palaeolithic sediments were studied palynologically come from four caves: Dzudzuana, Satsurblia, Kotias Klde and Bondi. Modern sediments were investigated from 6 caves. Fossil and modern samples were taken according to the standard procedure in palynology. The laboratory treatment was carried out as follows: first, 50 g of the sample was boiled in 10% KOH. At the second stage, centrifuging of the material in cadmium liquid was performed. At the final stage, acetolysis treatment was used.

Results: Pollen of *A. absinthium* L. (Asteraceae), *A. annua* L. (Asteraceae), *A. millefolium* L. (Asteraceae), *C. jacea* L. (Asteraceae), and *U. dioica* L. (Urticaceae) are identified to species level. This species are not edible and are popular in present-day folk medicine. In the Upper Palaeolithic layers, significant amounts of studies species pollen were recorded in the cave, likely due to their flowering branches being brought in by humans for use. Detailed consideration of the pharmacological characteristics of the examined species showed that almost all of them have anti-inflammatory, antibacterial, antimicrobial and antipyretic activity.

Conclusion: The fossil pollen complex of medicinal herbs, dominated by *A. millefolium* and *Artemisia* (*A. annua and A. absinthium*), suggests that the ancient population living in the studied caves could have been prone to malaria, rheumatism and gastrointestinal diseases. In the Upper Palaeolithic, the population inhabiting cave sites might have suffered from gout and callouses.

1. Introduction

Palynological studies of cultural layers of cave sediments make it possible to reconstruct palaeoecological conditions, due to the transport of large quantities of plant pollen and spores into the cave (Carrión, 1992; Carrión et al., 1999; Navarro et al. 2000, 2002; Arobba and Caramiello, 2009; Kvavadze et al., 2011, 2012). Palynological data are very important for inferring prehistoric uses of medicinal plants (Chaves and Reinhard, 2003). Pollen data have demonstrated that medicinal plants were used by Neanderthals around 60,000 cal. BP (Petrovska, 2012) and work at the archaeological site of Shanidar IV in present-day Iraq has shown that Middle Palaeolithic communities used many medicinal plants (Leroi-Gourhan, 1975; Lietava, 1992), including *Ephedra altissima* and *Centaurea solstitialis. Achillea*, *Muscari*-type, *Althae*-type, *Senecio*-type.

Pollen of medicinal plants has been found in archaeological material from other prehistoric sites worldwide (Merlin, 2003; Chaves and Reinhard, 2003; Eshleman, 2003; Martkopilshvili et al., 2012; Magyari et al., 2013). Yet there are very few data in the literature

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regarding the medicines used by Upper Palaeolithic humans (Roberts and Manchester, 1995; Chaves and Reinhard, 2003). To solve the problems of palaeopharmacology, caves are the most suitable object of study since Palaeolithic people used caves as dwellings and for storage of medicinal remedies.

The study of modern sediments of caves has shown that they predominantly contain pollen of anemophilous plants that can easily be transported by winds over long distances (Burney and Burney, 1993; Navarro et al., 2002; Eugenia de Porras et al., 2011). As for entomophilous taxa, their role is not very important in recent pollen spectra (Navarro et al., 2000; Kvavadze et al., 2011).

The presence of large quantities of entomophilous taxa in fossil spectra is therefore attributed to direct introduction by humans. Humans may have brought in edible plants, medicinal herbs, brushwood, branches and wood to make fire, moss polsters and leaves to cover the cave floor, etc.

In the foothills of Imereti (western Georgia) the palynological exploration of cave layers began in the 1980s and 1990s. In Dzudzuana cave, 19 samples taken from the Upper Palaeolithic layers were studied by David Lordkipanidze (Meshveliani et al., 1990). Though the palynological material was not very rich, the researcher could identify a rather long list of taxa which included pollen of medicinal plants (Meshveliani et al., 1990). Systematic studies of the Dzudzuana cave started in 2007 (Kvavadze et al., 2009b, 2010a; Meshveliani et al., 2010, 2011; Bar-Yosef et al., 2011) and have elevated Dzudzuana cave to a unique site of global significance since the discovery of twisted and dyed flax and wool fibres as old as 35,000–30,000 years (Kvavadze et al., 2009b, 2010a, 2011). These discoveries have significantly changed our understanding of the activity of Upper Palaeolithic humans, who were not only hunter-gatherers, but also might have been artisans.

The objective of the present publication is to investigate the range of medicinal plants found in the pollen spectra of the Upper Palaeolithic layers of karst caves in the western part of Georgia and are not edible and are popular in present-day folk medicine. However, the selection of taxa was also guided by the possibilities to identify species using light microscopy. We could unambiguously determine *Centaurea jacea* L. (Asteraceae), *Artemisia annua* L. (Asteraceae), *Artemisia absinthium* L. (Asteraceae), *Achillea millefolium* L. (Asteraceae), and *Urtica dioica* L. (Urticaceae), which allowed us to specify their curative properties.

The main goals of our research are: 1) to consider the pharmacological properties of medicinal herbs found in the cave sediments and their uses in modern and traditional medicine; 2) to establish the diseases typical for the Stone Age population based on modern pharmacological data for the species identified.

2. Material and methods

2.1. Material, recent environment and palaeoenvironment

The Upper Palaeolithic sediments we have studied palynologically come from four caves: Dzudzuana, Satsurblia, Kotias Klde and Bondi. Modern sediments were investigated from Samertskhle Klde, Khvedelidzeebis, Datvis, Dzudzuana, Satsrublia and Kotias Klde caves. Fossil and modern samples were taken according to the standard procedure in palynology (Moore et al., 1991). The need to study modern sediments inside and outside the cave is determined by the fact that we do not know how the pollen of different species is preserved (or not preserved) in the specific conditions (type of soil, microflora, climate, etc.). It should be noted that medicinal species such as *A. absinthium* L., *A. millefolium* L., *C. jacea* L and *U. dioica* L. grow in the neighbourhood of the caves studied. As ruderal (weedy) plants they follow human activity, growing in disturbed habitats along the roads and paths and other trampled places (Nakhutsrishvili, 2013). Pollen grains of the said medicinal species disperse readily over long distances.

The karst cave Dzudzuana is located near the village Darkveti of the Chiatura municipality at an altitude of 560 m a.s.l. (Fig. 1). The cave is located in a deep gorge closed in deciduous forest with predominance of hornbeam and oak. The climate here, as in whole of Imereti, is warm and humid. The average annual temperature is 13 °C and the average annual rainfall is 1100–1200 mm (Bondyrev et al., 2014).

In the cave, 5 profiles were made, from which 86 samples were taken and investigated palynologically. Each stratigraphic layer was studied and the absolute age of the whole sequence was defined by 23 radiocarbon readings (Meshveliani et al., 2006, 2010, 2011; Bar Yosef et al. 2011) covering the period from 36,000 to 6000 cal. BP. The palynological studies have shown that during the formation of the layer D the climate, on the whole, was cooler than during the formation of the layer C (Kvavadze et al., 2012). Unit D

Fig. 1. Map of Georgia (B) and location of investigated sites in the Imereti region (A): 1-Dzudzuana Cave; 2-Satsurblia Cave; 3-Kotias Klde Cave; 4-Bondi Cave; 5-Samerckhle cave; 6-Khvedelidzeebis Cave; 7-Datvis Klde Cave. Triangles indicate studied caves with Upper Palaeolithic layers; circles indicate caves where only modern sediments were investigated. Kutaisi is the capital of Imereti.

(36,000 – 31,000 cal. BP) represents the early Upper Palaeolithic Period, which comprises 21 samples. The upper limit of the birch and pine forest zone was situated near the cave at the time of deposition of layer D. The climate at this time appears to be cold and dry. Later, during the formation of layer C, the climate became warm and wet. Broad-leaved forests of oak, lime, walnut were growing in the vicinity of the cave. Wignut (*Pterocarya pterocarpa*), a good indicator of the warm climate, was growing in the river floodplain. During the formation of the layer B the climatic conditions became worse (LGM cooling), and dark coniferous high-mountain forests were spread around the cave (Kvavadze et al., 2012).

The Satsurblia karst cave is located in the Tskhaltubo region near the village Kumistavi at an altitude of 360 m a.s.l. (Fig. 1). Natural vegetation around the cave is almost entirely destroyed and occupied by crops of corn and other agricultural crops. Climatic conditions are very similar to those in the vicinity of Dzudzuana cave (Bondyrev et al., 2014).

In this cave, two profiles, as well as the second and the third floor layer dated to the Upper Palaeolithic, were studied (Meshveliani et al., 2013; Kvavadze et al., 2011; Pinhasi et al., 2014). The floor layers were dated between 17,895 – 16,215 cal. BP (Pinhasi et al., 2014). Altogether, 22 samples were investigated from Sarsurblia Cave and six samples of modern soils and moss were taken inside the cave and at its entrance. From this material 10 samples, dating of Upper Palaeolithic Period were chosen here, similar to the Dzudzuana environs, during climate warmings there grew broad-leaved forests. However, during the last glacial period (LGM) all the environs of the cave were occupied by coniferous forests (Pinhasi et al., 2014).

The cave Kotias Klde is located in the Chiatura region near the village Sveri at an altitude of 719 m a.s.l. and occupation levels are dated to 10,900 – 9940 cal. BP (Meshveliani et al., 2006). Landscapes around the cave are partially agricultural and partially covered with deciduous forests of hornbeam, oak, chestnut and beech. Clearings contain many azalea thickets (*Rhododendron luteum* Sweet). The climate is warm and humid (Bondyrev et al., 2014).

Altogether, 9 samples were obtained from the Upper Palaeolithic layers. In addition, samples of modern sediments were taken inside the cave, at the entrance, and around the cave. The pollen spectra of the material considered here documents that 11,000 – 10,000 years ago the climate around the cave Kotias Klde remained cool, since pine pollen is predominant.

The cave Bondi is 6 km away from Chiatura, by the village Tsirkvali (Fig. 1). Its elevation is 477 m a.s.l. The absolute age of the earliest layers is 38,700 – 35,000 cal. BP, while the upper layers (layer III) date to 26,600 – 14,000 cal. BP (Tushabramishvili et al., 2013). The cave is located on a bluff of the river Tabagrebi and the landscapes are domesticated, occupied by gardens and crops. The climate is warm and humid (Bondyrev et al., 2014).

It is a rather large karst cave and 11 samples (Profile 1 and floor) were taken from the Upper Palaeolithic layers and investigated (Tushabramishvili et al., 2009). The lowest layers VII–V corresponding to the layer D from the cave Dzudzuana also reflect colder climatic conditions when the cave was surrounded by coniferous forests with admixture of fir. The upper layers formed during the LGM cooling were distinguished by more severe climatic conditions, and in the landscape, spruce and pine became more important.

2.2. Method

The laboratory treatment was carried out as follows: first, 50 g of the sample was boiled in 10% KOH. The solution was washed with distilled water and settled. At the second stage, centrifuging of the material in cadmium liquid was performed. At the final stage, acetolysis treatment was used. Identification and counting of the material was conducted in glycerine on a light photomiscroscope Olympus BX43 with magnifications up to 1000 ×.

Existing atlases, publications and comparative collections of recent material were used in identification. The determination of

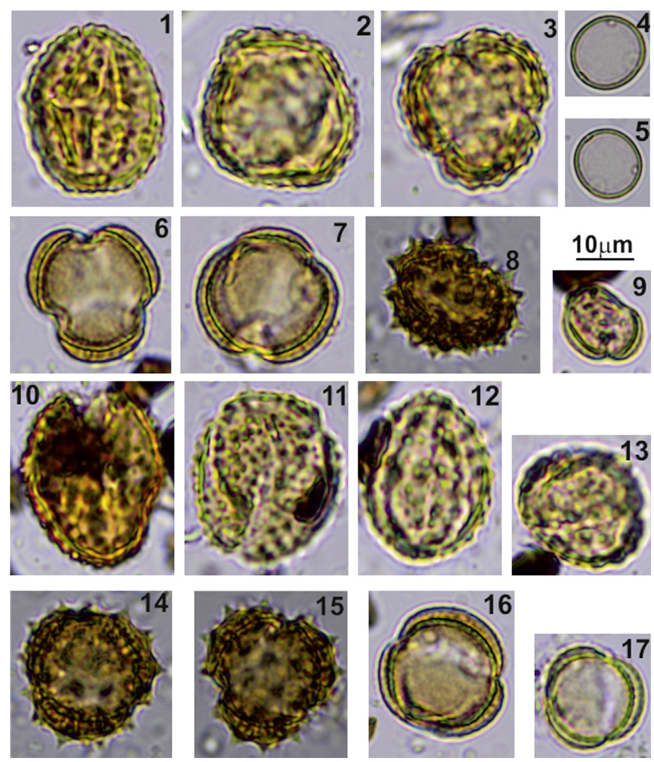

Fig. 2. Pollen of investigated medicinal plants: 1,2,3-*Centaurea jacea* from Satsurblia Cave; 4,5-*Urtica dioica* from Satsurblia Cave; 6,7-*Artemisia absinthium* from Bondi Cave; 8-*Achillea millefolium* from Dzudzuana Cave; 9-*Artemisia annua* from Dzudzuana Cave;10- *Centaurea jacea* from Bondi Cave; 11,12-*Centaurea jacea* from Kotias Klde Cave; 13-*Centaurea jacea* from Dzudzuana Cave;14,15-*Achillea millefolium* from Kotias Klde Cave; 16-*Artemisia absinthium* from Kotias Klde Cave; 17-*Artemisia annua* from Satsurblia Cave.

Table 1
Abundance of pollen in modern pollen spectra.

Caves	*Achillea millefolium L.*		*Centaurea jacea L.*		*Urtica dioica L.*		*Artemisia*	
	Inside	Outside	Inside	Outside	Inside	Outside	Inside	Outside
Dzudzuana Cave	2	9	1	2		1	1	1
Satsurblia Cave		3		4		7	1	4
Kotias Klde Cave		7		2		2		16
Khvedelidzeebis Cave	11	25	7	11	3	10	1	15
Samertskhle Klde Cave	7	22	1	4		2		3
Datvis Cave		4		5		2		2
Total sum of pollen	20	70	9	28	3	24	3	41

C. jacea is based on descriptions and micrographs of pollen grains from pollen atlases of Reille (1992) and Beuh (2004). The morphology of pollen grains from *A.a annua, A. absinthium, A. millefolium, U. dioica* is described in detail by various authors (Kuprianova and Alyoshina, 1978; Reille, 1992; Beuh, 2004). To plot the diagrams, the "Tilia" software (Grimm, 2004) was used. In all block-diagrams (Figs. 3–6) the absolute abundances (number of pollen grains) are shown. The relative abundances shown in Figs. 7 and 8 are based on the pollen sum of the five species investigated in this study.

2.3. Characteristics of pollen spectra of modern sediments inside and outside the caves

Modern samples have been studied from the Dzudzuana, Satsurblia, and Kotias Klde, caves that also contain archaeological material. Surface samples have also been taken from another three karst caves in the same region: Khvedelidzeebis, Samercxle and Datvis Klde caves (Fig. 1). The results of palynological studies are shown in Table 1 and Fig. 2. The presence of five important medicinal species – *A. absinthium* L. (Asteraceae), *A. annua* L. (Asteraceae), *A. millefolium* L. (Asteraceae), *C. jacea* L. (Asteraceae), and *U. dioica* L. (Urticaceae) – in the landscapes of the region is recorded perfectly in the palynological spectra of the samples from outside the caves. However, as for the modern spectra of the samples taken from within the caves, they are either not reflected or the amount of pollen is strongly underestimated. The presence of nettle (*U. dioica*) pollen is especially poorly recorded in the palynological spectra of the caves, although in soils and mosses around the caves Satsrublia and Khvedelidzeebis its pollen was found in fairly large amounts (Table 1). Wormwood pollen (from the few species of *Artemisia*) is also poorly reflected in the spectra inside the cave, but in the subfossil spectra outside the cave its pollen is rather well represented. The quantity of *A. millefolium* pollen and *C. jacea* pollen grains are also three and four times lower inside the caves compared to outside.

Thus we can conclude that: 1) nettle (*U. dioica*) pollen is generally not transported into caves by wind in the study region and is most abundant directly near source plants; 2) *Artemisia* pollen is also very poorly dispersed; 3) the majority of the yarrow (*A. millefolium*) and knapweed (*C. jacea*) pollen (70–80%) is also accumulated near populations of these plants.

Poor wind-dispersal of pollen grains of *Achillea* and *Urtica* as well as of *Centaurea* and *Artemisia* in the humid zones of the Caucasus is indicated not only by sub-recent spectra of soils and mosses (Stuchlik and Kvavadze, 1987), but also by the results of pollen monitoring conducted in Georgia since 1996 (Kvavadze, 1999, 2001; Hicks et al., 2001; van der Knaap et al., 2010; Kvavadze et al., 2009a).

3. Archaeological and palynological results from Palaeolithic layers

3.1. Cave Dzudzuana

In this cave, there are four stratigraphic layers belonging to the Palaeolithic and the Upper Eneolithic (Bar-Yosef et al., 2011). Unit D (36,000 – 31,000 cal. BP) represents the early Upper Palaeolithic toolkit of unidirectional short blades and small bladelets. The lithic industry in Unit C (27,000 – 24,000 cal. BP) is dominated by small bladelets detached from carinated cores. Unit B (16,000 – 13,000 cal. BP) is rich in blades and bladelets removed from bipolar cores, shaped into microgravettes, elongated straight-backed items and numerous end scrapers. Unit A (6000 – 5000 cal. BP) represents admixture of Late Neolithic/Eneolithic and historical occupations. All the units contain worked bone artifacts, including a perforated needle from Unit C, as well as groundstone utensils and faunal remains.

During the accumulation of layers D and C in Dzudzuana Cave, humans occupied the cave for a sustained period and, in addition to the abundance of stone tools, numerous charred tracheal cells of wood left after the fire, as well as fibres of flax yarn or textile were found (Bar-Yosef et al., 2011). However, at the boundary of the D and C layers (after 27,000 cal. BP) a significant deterioration of climatic conditions is observed (Kvavadze et al., 2012). Archaeological and palynological data suggest that during the said cooling, humans abandoned the cave. The cave was then occupied by wild animals, whose presence was recorded in the spectra by spores of coprophilous fungi and microscopic remains of mites and insects that parasitized on animals (Kvavadze et al., 2010b).

During the formation of the upper part of layer C, the climate again warmed, and humans returned to Dzudzuana Cave (Bar-Yosef et al., 2011). In Unit D and the upper part of Unit C, textile fibres, tracheal cells of burnt wood and *Pooidea* phytoliths indicate that humans lived in the cave. Pollen spectra of this period contain a significant amount of *A. absinthium* L., *A. annua* L., *A. millefolium* L., *C. jacea* L., and *U. dioica* L. pollen (Figs. 2 and 3). Pollen grains of these plants are observed in all five studied profiles. In this paper we give the results for the profile where, on the whole, the highest amount of plant pollen and spores have been counted. The pollen diagram of profile II (Fig. 3) clearly shows that more intensive habitation of the cave occurred during the accumulation of the upper part of the layer D. Here, the increase in pollen of edible plants and medicinal herbs is clearly seen. For example, the quantity of pollen of wild grasses eaten by people increases. *Carduus* (its young green twigs are sweet and juicy), *Polygonum*

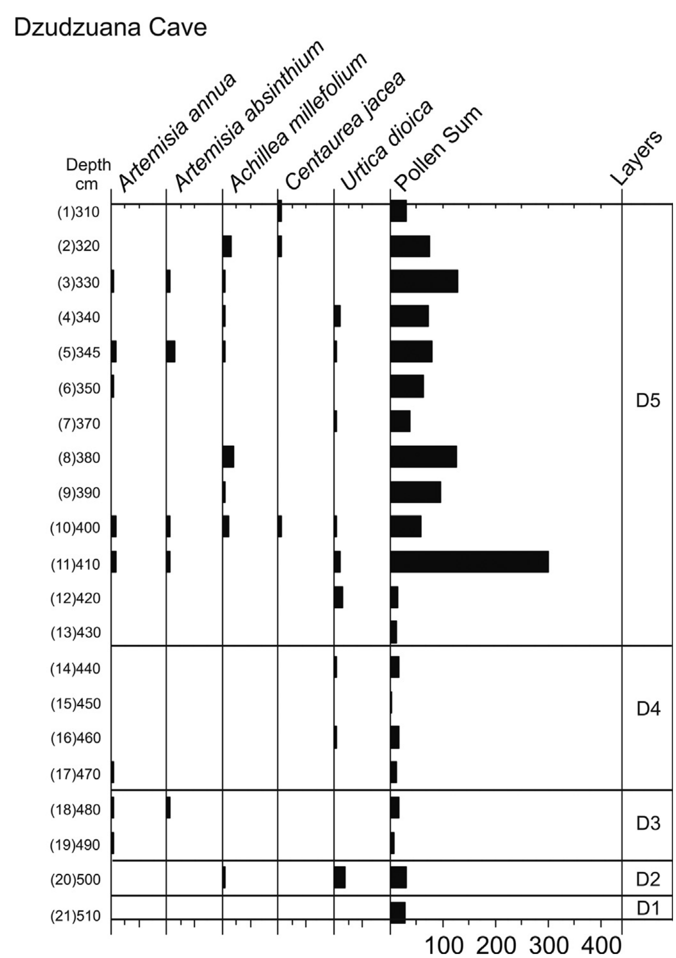

Fig. 3. Absolute abundances of pollen from the investigated species in Profile II from Dzudzuana Cave; the right column gives the total sum of pollen grains in the samples.

and Chenopodiaceae are also edible. In the D-5 layer, the content of hazel (*Corylus*), walnut (*Juglans*) and vine (*Vitis*) pollen increases, since these plants were also part of the diet of Stone Age communities.

3.2. Cave Satsurblia

In this cave, 22 samples have been studied, but in this paper we give the results only for 10 studied samples (from the Upper Palaeolithic layers). Their pollen spectra also contain medicinal herbs, including *C. jacea* L., *A. annua* L., *A. absinthium* L., *A. millefolium* L. and *U. dioica* L. (Fig. 4). *U. dioica* pollen grains were also found in the second and the third floor layers (Pinhasi et al., 2014). In these samples, the amount of pollen of edible plants (hazelnut, chestnut, beech, wild grasses, etc.) increases, which shows that during the accumulation of the layers from which samples 16 and 19 were taken, humans had been living in the cave for quite a long time. The continued presence of humans, in addition to the archaeological and palynological material, is also recorded by an increase in the amount of flax textile fibres and charred tracheal cells of wood left after fires.

3.3. Cave Kotias Klde

Pollen of many medicinal plants is well represented in the Upper Palaeolithic layers of the cave Kotias Klde (Fig. 5).

In the Upper Palaeolithic layers, the maximum content of *C. jacea*, *A. annua*, *A. absinthium*, *A. millefolium* and *U. dioica* pollen is observed in samples 5 and 6. Here, there are also large quantities of pollen of edible plants and especially of chestnut (*Castanea*), hazel (*Corylus*), walnut (*Juglans*) and wild grasses (Poaceae), which indicates human habitation in the cave for prolonged periods.

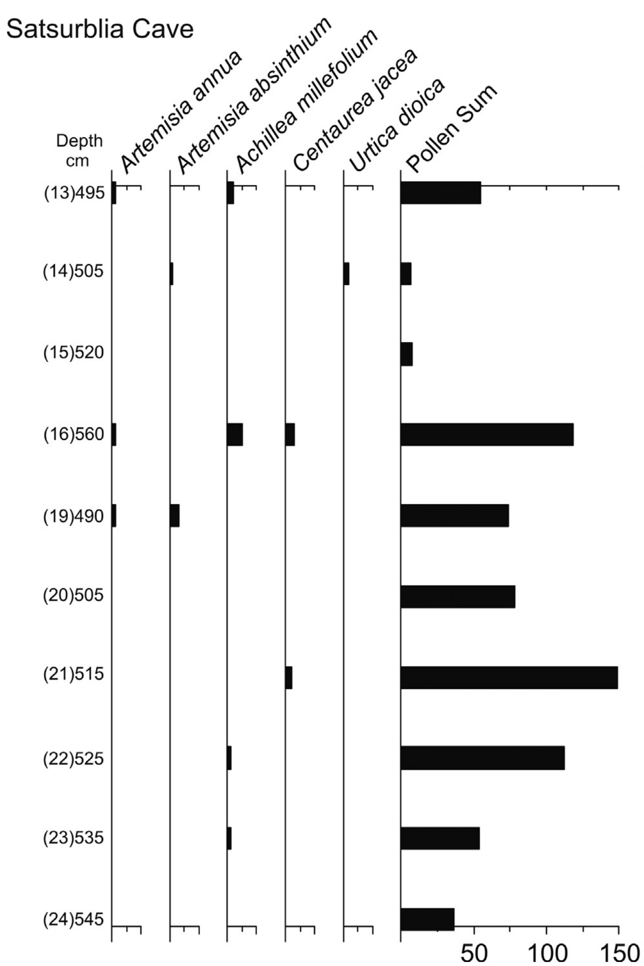

Fig. 4. Absolute abundances of pollen from the investigated species in the Upper Palaeolithic layers of Satsurblia Cave; the right column gives the total sum of pollen grains in the samples.

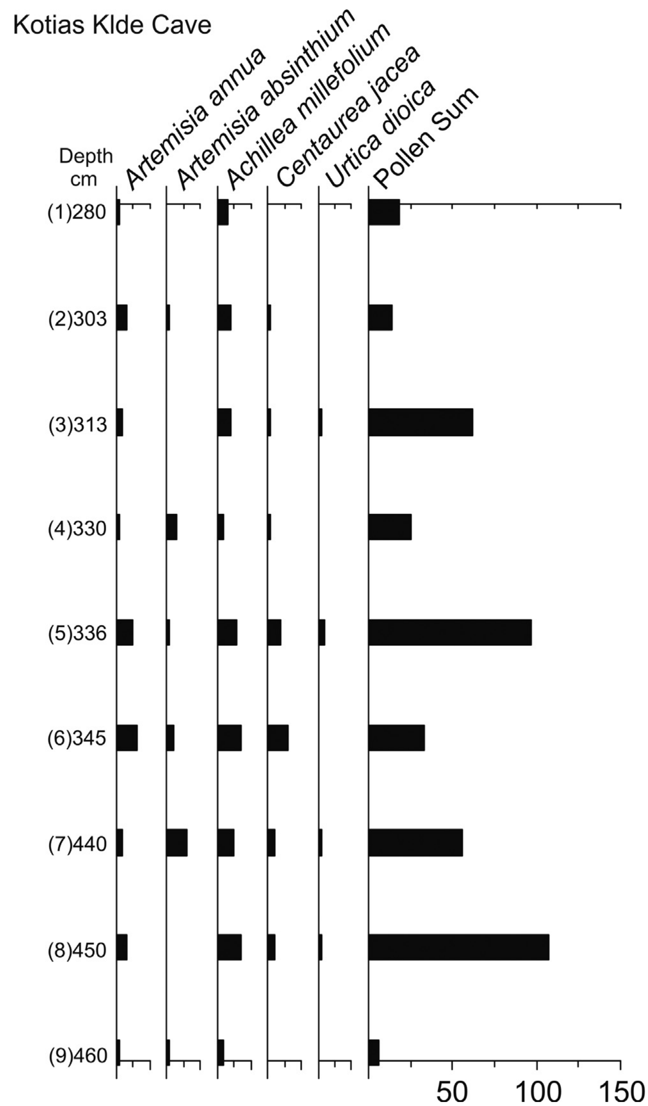

Fig. 5. Absolute abundances of pollen from the investigated species in the Upper Palaeolithic layers of Cave Kotias Klde; the right column gives the total sum of pollen grains in the samples.

3.4. Cave Bondi

Despite the fact that this karst cave contained rather small quantities of pollen (Tushabramishvili et al., 2009), medicinal plant pollen grains were found in nearly all studied layers (Fig. 6). Wormwood (*A. annua*) pollen was recorded in the bottom and top layers of the profile. Yarrow (*A. millefolium*) and brown knapweed (*C. jacea*) are better represented in top layer 2. Pollen grains of nettle (*U. dioica*) were not found at all, which might be explained by poor conditions of pollen preservation. Of edible plants, the pollen of wild grasses (Poaceae), hazel (*Corylus*), dogwood (*Cornus*), buckwheat (*Polygonum aviculare*, *Polygonum*-type) was found in the Upper Palaeolithic layers of Bondi cave. In the layers accumulated during the long human habitation, an increase in the amount of flax and wool textile fibres and tracheal cells of charred wood is observed. These non-pollen palynomorphs belong

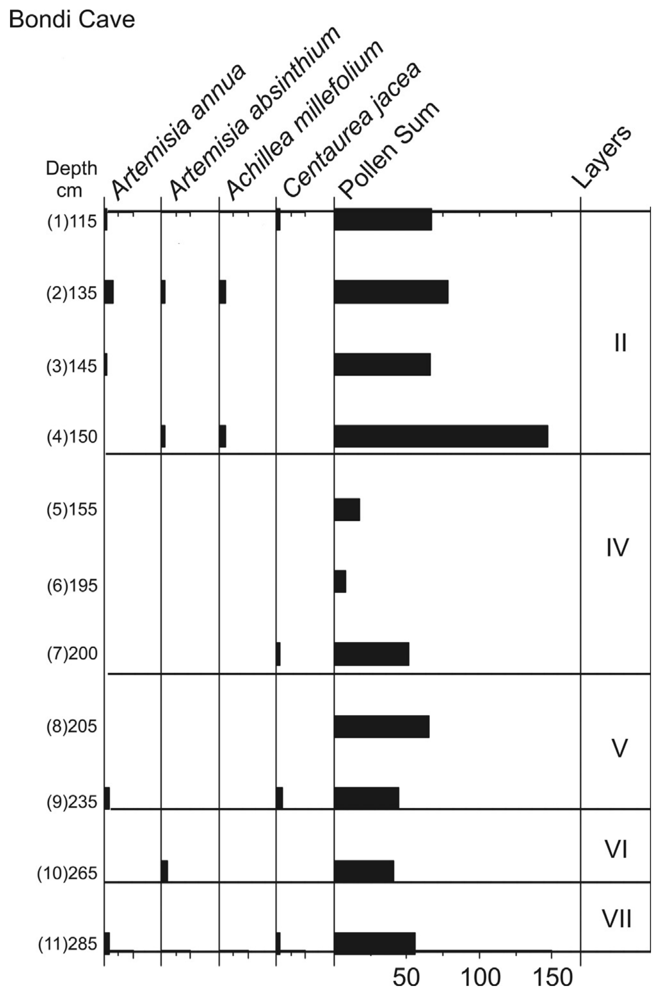

Fig. 6. Absolute abundances of pollen from the investigated species in the Upper Palaeolithic layers of Bondi Cave; the right column gives the total sum of pollen grains in the samples.

to the group of anthropogenic indicators (Tushabramishvili et al., 2009, 2013).

4. Some phytochemical and pharmacological data on the studied species

4.1. *Achillea millefolium L.*

A. millefolium L. prefers open and dry slopes, though it also grows near human dwellings, along the roads and in waste places. It is considered a ruderal plant (Radusiene and Gudaityte, 2006; Gagnidze, 2007; Nakhutsrishvili, 2013). The main pharmacological components of *A. millefolium* are flavonoids, phenolic acids, alkaloids, terpens (cineol, borneol, pinens, camphor, azulen), tannins, cis-Carveol, achillin and leucosis (Shahbazi and Zadeh, 2008; Bimbirait et al., 2008; Raju et al., 2009; Lakshmi et al., 2011; Feizpour et al. 2013). Flavonoids and phenol carbonic acids of yarrow constitute the most important groups of pharmacologically active substances (Shahbazi and Zadeh, 2008; Bimbirait et al., 2008; Raju et al., 2009; Lakshmi et al., 2011; Feizpour et al., 2013). The most noticeable effects of this plant are on antioxidant and antimicrobial activity (Candan et al., 2003; Lakshmi et al., 2011); anti-inflammatory (Goldberg et al., 2006); antihypertensive, bronchodilatory, (Khan and Gilani, 2011), gastrointestinal antispasmodic (cramps, indigestion, epigastric distension, flatulence, and intestinal colic), (Benedek and Kopp, 2007; Lakshmi et al., 2011), diuretic, urinary antiseptic (Bag et al., 2008) and astringent and antihemorrhagic effects (Işcan et al., 2006).

According to the traditions of folk medicine, *A. millefolium* is mainly used for the treatment of gastrointestinal diseases, anaemia and as antistyptic (Odisharia and Sabakhtarashvili, 1993; Chevallier, 1996; Moerman, 1998; Menković et al., 2011; Zlatović et al., 2014; Jamila and Mostafa, 2014). According to other authors, yarrow treats diabetes, hypertension and can be used as an antimicrobial agent (Said et al., 2002; Hassawi and Kharma, 2006). It has also traditionally been used as an abortifacient, emmenagogue, contraceptive, and for stimulating uterine contractions (Lakshmi et al., 2011). For this reason, it is contra-indicated for use in pregnancy. There has, however, been little scientific research (Lakshmi et al., 2011).

4.2. *Artemisia annua L.*

A. annua L. as a medicinal plant was first investigated in 1971 in China, and the medicine made from it had the name artemisinin (White, 2008). Artemisinin is a key-ingredient in the leading treatment for malaria and is an extract of an ancient medicinal plant. The re-discovery of *A. annua* as a medicinal plant reveals something that Dalrymple (2008) calls a "golden triangle" – an interaction between traditional medicine, modern medicine and science (Mueller et al., 2004; Ferreira, 2004; Mamedov and Craker, 2008; Adams et al., 2009; Meier zu Biesen, 2010). *A. annua* produces at least 36 flavonoids. Many of these have antimalarial activity *in vitro*, although the inhibitory concentration is 50% (IC50). Five of these, artemetin, casticin, chrysoplenetin, chrysosplenol-D, and cirsilineol, have been shown selectively to affect the *in vitro* activity of artemisinin against *Plasmodium falciparum* (Liu et al., 1992). The effect of all the flavones in combination with artemisinin has not yet been investigated. Other flavones, and indeed other components of *A. annua*, may have a similar effect; they have not all been tested because it is difficult to purify them. The antimalarial properties of the traditional preparation of *A. annua* most probably reside in the combination of many constituents, not just artemisinin (see Willcox et al., 2004). The fact that artemisinin-based combination therapies are 'ancient' in their use and 'modern' in their formulation shows the transformative potential of the plant itself (see Meier zu Biesen, 2010).

4.3. *Artemisia absinthium L.*

A. absinthium L. is a ruderal plant (Radusiene and Gudaityte, 2006; Gagnidze, 2007; Nakhutsrishvili, 2013). Flavonoids, tannins, glucosides, carotenoids, andphenolic compounds are major phytoconstituents of *A. absinthium* (Nikhat et al., 2013). Flavonoids components include quercitin 3-glucoside and 3-rhamnoglucoside, spinacetin 3-glucoside and 3-rhamnoglucoside (Nikhat et al., 2013). One drug derived from wormwood is Afsantin, which has been reported as an anti-inflammatory, antipyretic, hepatoprotective, antidepressant, antioxidant, deobstruents, analgesic, antiseptic and antimicrobial (Dettling et al., 2004; Lopes-Lutz, 2008; Carner, 2008; Movilla Pires, 2009; Mahmoudi et al., 2009; Tariq, 2009; Amat and Upur, 2010; Karabegoviæ, 2011; Singhal and Gupta, 2012; Saxena and Shukla, 2012; Efferth, 2014). Owing to these properties, it has been used to treat various diseases, such as atherosclerosis, cardiovascular diseases, fever, abdominal pain, intestinal worms, cognitive dysfunctions, hepatitis, malarial fever, cancer and rheumatism (Halliwell, 1997; Nikhat et al., 2013; Menale and Muoio, 2014). Research shows that it is highly effective and carries a low risk of toxicity and side effects. There is a need to scientifically establish its efficacy and safety in order to achieve global acceptance (Nikhat et al., 2013).

4.4. *Centaurea jacea* L.

In the Caucasus *C. jacea* generally grows on forest edges and in clearings (Agababyan and Fajvush, 1991; Agababyan, 1997; Gagnidze, 2007; Nakhutsrishvili, 2013).

Different types of secondary metabolites (flavonoids, sesquiterpenes) were found to be responsible for the anti-tumour effects of extracts of *C. jacea*; the highest activity was exerted by centaureidin, in addition to moderately active compounds: cirsiliol, isokaempferide, apigenin, hispidulin, cnicin and 4′-acetylcnicin (Forgo et al., 2012). The chloroform extract of *C. jacea* afforded the isolation of cirsiliol, apigenin, hispidulin, eupatorin, isokaempferide, axillarin, centaureidin, 6-methoxykaempferol 3-methyl ether, trachelogenin, cnicin, 4′-acetylcnicin and three aliphatic glucose diesters, including the new natural product 1β-isobutanoyl-2-angeloyl-glucose (Forgo et al., 2012).

In the Turkish folk medicine *C. jacea* was particularly recommended against inflammatory conditions and to reduce fever (Yesilada, 2002).

Other species of *Centaurea* have been used in traditional medicine as a diuretic and to treat fever and diabetes (Font Quer, 1995). Many *Centaurea* were added to tonics in the belief that they stimulate the flow of saliva and stomach acids, returning appetite to invalids (Bernhardt, 2008). *Centaurea* species are famous in folk medicine to have anti-diarrheic, anti-dandruff, anti-rheumatic, anti-inflammatory, cholagogue, choleretic, digestive, stomachic, menstrual, astringent, hypotensive, anti-pyretic, cytotoxic as well as anti-bacterial effects and are used alone or mixed with other plants (Farrag et al., 1993; Barrero et al., 1997; Orallo et al., 1998; Köse et al., 2007).

4.5. *Urtica dioica* L.

U. dioica L. (nettle), being a ruderal species, grows in trampled, shaded areas along paths and near human dwellings (Gagnidze, 2007; Nakhutsrishvili, 2013). Nettle leaves contain 1–2% flavonoids, (particularly glycosides and rutosides of quercetin, kaemferol and isohamnetin). The herbal substance contains silicates in a relatively large quantity (1–4% SiO_2) partly as water-soluble silicates. Characteristic components are scopoletin, sitosterol with its 3-O-βD-glucoside and caffeic acid esters. Other constituents include chlorophyll (approximately 2.7%), proteins, fats, carbohydrates, traces of nicotine and, in the stinging hairs, small amounts of acetylcholine, serotonin, formic acid and leukotrines (Asgarpanah and Mohajerani, 2012; Wichtl, 2002). According to other authors, alkaloids, tannins and terpenoids are present in nettles (Kais Kassim Ghaima et al., 2013). The available literature shows that *U. dioica* L. has antioxidant (Kanter et al., 2005), anti-inflammatory (Hajhashemi and Klooshani, 2012), anti-ulcer (Gülçin et al., 2004), anticancer, antimicrobial (Nisha et al., 2011), cardiovascular (Asgarpanah and Mohajerani, 2012) and hepatoprotective (Kanter et al., 2005) properties.

U. dioica is considered a good remedy for rheumatism, asthma, anaemia and gout (Launert, 1981; Foster and Duke, 1990; Adams et al., 2009; Hayta et al. 2014; Zlatović et al., 2014). Moreover, nettles are used to treat burns, viral, bacterial and fungal diseases (Foster and Duke, 1990; Adams et al., 2009). Nettle is also a good pain reliever for rheumatism (Randall et al., 1999; Bown, 1995; Hajhashemi and Klooshani, 2012). New investigations showed that these recent results confirm the folkloric use of the plant extract to treat painful and inflammatory conditions. Further studies are needed to characterise the active constituents and the mechanism of action of the plant extract (Hajhashemi and Klooshani, 2012).

5. Discussion

The study of modern spectra of cave sediments inside and outside the cave and the significant representation of *C. jacea* L., *A. annua* L., *A. absinthium* L., *A. millefolium* L. and *U. dioica* L. pollen showed that pollen grains of these species in the study region are not always transported by wind over long distances. Therefore the amount of their pollen in present-day caves tends to be very small. However, they are quite well represented in the palynological spectra of sediments taken outside the cave. In this regard, the substantial presence of pollen from medicinal species – *C. jacea, A. annua, A. absinthium, A. millefolium* and *U. dioica* – in the Upper

Table 2
List of medicinal plant species (which pollen found in Upper Palaeolithic sediments) used in traditional medicine.

Species	Pharmacological properties	Use in folk medicine	Reference
Artemisia annua L.	Anti-malarial activity	Malaria	Liu et al., 1992; Ferreira, 2004; Mueller et al., 2004; Willcox et al., 2004; White, 2008; Dalrymple, 2008; Mamedov and Craker, 2008; Adams et al., 2009; Meier zu Biesen, 2010.
Artemisia absinthium L.	Anti-malarial, anti-inflammatory, antipyretic, hepatoprotective, antiseptic, antimicrobial, analgesic, anti-rheumatic, cancer, cardiovascular, atherosclerosis	Rheumatism, atherosclerosis, fiver, pain abdomen, malaria fever, hepatitis, cancer	Halliwell, 1997; Dettling et al., 2004; Radusiene and Gudaityte, 2006; Lopes-Lutz, 2008; Carner, 2008; Mahmoudi et al., 2009; Movilla Pires, 2009; Tariq, 2009; Amat and Upur, 2010; Karabegoviæ, 2011; Saxena and Shukla, 2012; Singhal and Gupta, 2012; Nikhat et al., 2013; Efferth, 2014; Menale and Muoio, 2014.
Achillea millefolium L.	Anti-inflammatory, antimicrobial, antioxidant, antihypertensive, bronchodilator, antibacterial, gastrointestinal, antispasmoic, antidepressant, diuretic, urinary antiseptic, astringent, anti-hemorrhagic effect, abortifacient.	Gastrointestinal diseases, anaemia, anti-styptic, diabetes	Odisharia and Sabakhtarashvili, 1993; Chevallier, 1996; Moerman, 1998; Said et al., 2002; Goldberg et al., 2006; Hassawi and Kharma, 2006; Işcan et al., 2006; Radusiene and Gudaityte, 2006; Benedek and Kopp, 2007; Bag et al., 2008; Shahbazi and Zadeh, 2008; Bimbirait et al., 2008; Candan et al., 2003; Raju et al., 2009; Khan and Gilani, 2011; Lakshmi et al., 2011; Menković et al., 2011; Feizpour et al., 2013; Jamila and Mostafa, 2014; Zlatović et al., 2014.
Centaurea jacea L.	Anti-inflammatory, anti-diuretic, antidandruff, anti-rheumatic, antipyretic, antibacterial, choleretic, digestive, stomachic.	Inflammatory conditions and to reduce fever, diuretic, diabetes	Agababyan and Fajvush, 1991; Farrag et al., 1993; Font Quer, 1995; Agababyan, 1997; Barrero et al., 1997; Orallo et al., 1998; Yesilada, 2002; Köse et al., 2007; Bernhardt, 2008; Forgo et al., 2012.
***Urtica dioica* L.**	Anti-inflammatory, antioxidant, antiulcer, anti-cancer, antimicrobial, cardiovascular, hepatoprotective.	Rheumatism, asthma, anaemia, gout, fungal diseases.	Launert, 1981; Foster and Duke, 1990; Bown, 1995; Randall et al., 1999; Gülçin et al., 2004; Wichtl, 2002; Kanter et al., 2005; Adams et al., 2009; Nisha et al., 2011; Asgarpanah and Mohajerani, 2012; Hajhashemi and Klooshani, 2012; Kais Kassim Ghaima et al., 2013; Hayta et al., 2014, Zlatović et al., 2014.

Palaeolithic layers of the caves is best explained by the fact that humans brought their flowering branches inside for their needs. Thus, the presence of *C. jacea, A. annua, A. absinthium, A. millefolium* and *U. dioica*, established by the pollen found in the cultural layers in all four studied Upper Palaeolithic caves, may help to reveal many details of palaeopharmacology and diseases of prehistoric humans. As already noted, there are currently very few data on Upper Palaeolithic palaeopharmacology, so palynology is very important for finding solutions to this problem (Chaves and Reinhard, 2003). The overview of the literature on the therapeutic properties of the studied plants shows a fairly wide range of applications for all five species (Table 2). Nettle (*U. dioica*) is unique as it has the largest number of indications for treating many (about 14) diseases (Kais kassim Ghaima et al., 2013). Yarrow (*A. millefolium*) has more than 11 pharmacological properties. The common pharmacological characteristics of the studied species provide insights into the prevailing medical conditions among the cave's Palaeolithic population. For example, all species except *A. annua* have an anti-inflammatory activity. Antibacterial, antimicrobial and antipyretic activities are also common traits (Plate 2) for these species. On the whole, the five studied species can treat a very large number of diseases. It is probable that 35–25 thousand years ago, people might have known the medical properties of these species, collected them and used them for treating illnesses.

In the Dzudzuana cave, *U. dioica*, according to palynological data, was an important remedy in the Upper Palaeolithic (Fig. 7a); it accounts for 35% of the total counted pollen of the five studied species.

In the cave Satsurblia, the content of nettle pollen grains is 15%, but in the layers of the Kotias Klde cave, this figure does not exceed 6%, and in the Bondi cave nettle pollen is not found at all (Fig. 7b). It should also be noted that the people could not eat raw, unprocessed nettle because of its sting. The lack of pottery suggests that nettle could not be cooked. However, there were stone mortars and cups, one of which was found in the Dzudzuana cave (Meshveliani et al., 2009), which were used to grind not only nettle, but also many seeds, roots and fruits of medicinal plants. This mortar-ground nettle was probably applied to wounds or aching joints.

In folk medicine, nettle (*U. dioica*) is considered to be a good remedy for rheumatism, asthma, anaemia and gout (Launert, 1981; Foster and Duke, 1990; Adams et al., 2009; Hayta et al., 2014; Zlatović et al., 2014). Moreover, in folk medicine, nettle is often used to treat burns, viral, bacterial and fungal diseases (Foster and Duke, 1990; Adams et al., 2009). Nettle is also a good pain reliever for rheumatism (Randall et al., 1999; Bown, 1995; Hajhashemi and Klooshani, 2012). It should be mentioned here that, besides nettle, antirheumatic properties are also characteristic for the medicinal plant *A. absinthium,* which was also found in the layers of the Dzudzuana cave and accounts for 4% of the pollen. *A. annua* content reaches 26% in the same layers. Antimalarial activity is a common trait in the pharmacological properties of these two wormwood species (Table 2). This may indicate that the ancient inhabitants of Dzudzuana, besides rheumatism, also suffered from malaria. In the Dzudzuana layers, *A. millefolium* pollen content is rather high and accounts for 28%. This plant differs from all other studied species by having gastrointestinal antispasmodic properties. Yarrow is also a good antidepressant (Table 2).

According to the tradition of folk medicine, yarrow is mainly used for the treatment of gastrointestinal diseases and anaemia (Odisharia and Sabakhtarashvili, 1993; Chevallier, 1996; Moerman, 1998; Menković et al. 2011; Zlatović et al., 2014; Jamila and Mostafa, 2014). According to other authors, yarrow treats diabetes and hypertension and can be used as an antimicrobial agent (Said et al., 2002; Hassawi and Kharma, 2006).

As for the *C. jacea* pollen grains, their content is not high, and reaches only 7%. Brown knapweed is used in folk medicine as a remedy to reduce fever, diabetes, anaemia, cholecystitis, gastritis and as an antifungal agent (Yesilada, 2002; Said et al., 2002; Khammar and Djeddi, 2012).

Based on the quantitative composition of the studied species, we can conclude that the ancient population of Dzudzuana cave suffered from several diseases, with a predominance of rheumatism, malaria, asthma and gastric diseases.

In the cultural layers of the Satsurblia cave, *A. millefolium* pollen is predominant and accounts for 45% of the content of all five species (Fig. 7b). This may indicate that the ancient population of the Satsrublia neighbourhood was in greater need of this remedy. Yarrow, as already noted, is used in folk medicine mainly to treat gastric diseases. Yarrow is also a urinary antiseptic and diuretic (Table 2).

In the Upper Palaeolithic layers of Satsurblia cave, the second dominant after yarrow pollen is *C. jacea* (25%), which treats gastritis, anaemia, reduces fever and diabetes (Table 2). The pollen of two species of wormwood (Fig. 7b) accounts for 15% (10% *A. annua* and 5% *A. absithium*). The presence of *Artemisia* pollen suggests the existence of malaria and rheumatism in the Satsurblia area. The population might have treated rheumatism using nettle, the pollen content of which is 15% (Fig. 7b).

The percentage of pollen of medicinal plants in the Upper Palaeolithic layers of the Kotias Klde cave is noteworthy. Here *A. millefolium* pollen is predominant and accounts for 46% (Fig. 7c). This means that the local population had a great need for yarrow, i.e. stomach and urological diseases may have been widespread here. *C. jacea* was also collected and stored; in the palynological spectra it accounts for 20%. The content of *A. annua* is slightly less than the brown knapweed and accounts for 18%. The share of *A. absinthium* is 9%. Nettle pollen was not found in large quantities (6%).

The palynological spectra of the Bondi cultural layers (Fig.7d) are dominated by *A. annua* pollen (58%). The second most prevalent is *A. millefolium* (19%). *C. jacea* pollen accounts for 14%. Large amounts of *A. annua* collected and used by the Bondi population may be explained by the widespread occurrence of malaria at that time. This would have been facilitated by its proximity to the river, the banks of which might have been swampy. *A. millefolium* and *C. jacea* were used to treat other diseases mentioned above

Thus, summarizing the data for all studied caves, we can see that the Upper Palaeolithic population used a great deal of yarrow (Fig. 8), which in modern medicine, as noted above, treats more than 14 diseases. *A. annua* was also extensively used.

A comparison of the total amount of pollen of the five examined genera in the studied caves (Fig. 8) shows that they have different quantities of wormwood (*A. annua* and *A. absinthium*), yarrow (*A. millefolium*), nettle (*U. dioica*) and brown knapweed (*C. jacea*) pollen. The question arises: what caused such a significant difference in the percentage of medicinal herbs in the above four caves? For example, why was nettle more widely used by ancient people living in the Dzudzuana cave than by residents of other caves? The reasons could certainly be different. Primarily, the said plant genera, depending on local geographical conditions in the surrounding environment, may have had a different distribution. Nettle (*U. dioica*), being a ruderal species, grows in trampled, shaded areas along paths and near human dwellings. Animals do not usually eat it, and therefore its thickets develop quite rapidly.

A. millefolium grows perfectly on pastures, and owing to its strong smell, it is not eaten by herbivores. Animals do not eat any species of *Artemisia*, since this plant is bitter. Being a ruderal plant, it grows abundantly in trampled places, along the roads and paths and near human dwellings. As for *C. jacea*, it grows on forest edges and clearings (Agababyan and Fajvush, 1991; Agababyan, 1997; Gagnidze, 2007; Nakhutsrishvili, 2013).

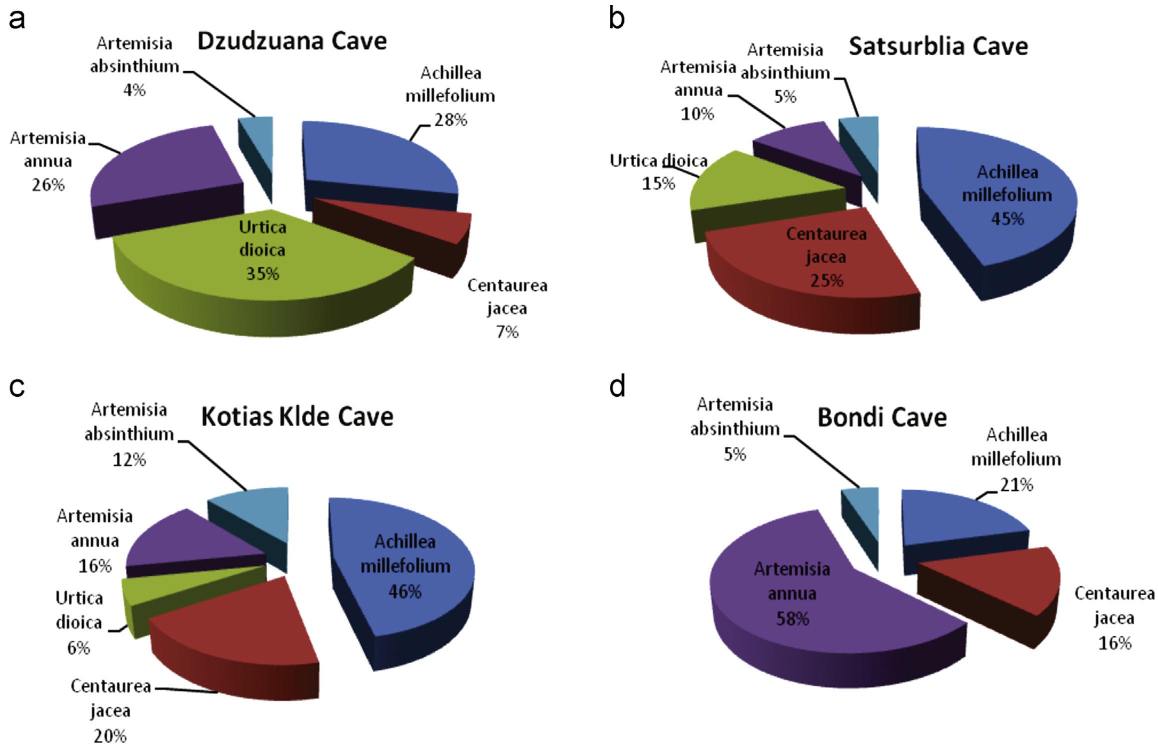

Fig. 7. Relative abundances of pollen from the investigated medicinal plants in the different caves; a-Dzudzuana Cave; b-Satsurblia Cave; c- Kotias Klde Cave; d-Bondi Cave.

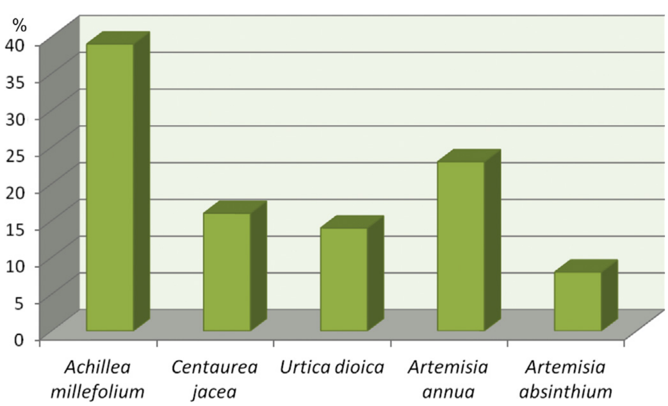

Fig. 8. Total relative abundances of pollen from the investigated medicinal plants summed up for all investigated caves.

Local geomorphological and geographical conditions could also have influence on the nature of the most common diseases of the population in the late Palaeolithic. For example, even at present, the humid climate in western Georgia (and especially in Imereti due to the proximity of the Black Sea and the western transport of air masses) causes rheumatism and arthritis in the local population. Until the advent of appropriate medicines and mosquito control programmes, malaria was widespread in the study region. In our opinion, these diseases existed in the Upper Palaeolithic, since in the identified set of medications there were plants for treating malaria and rheumatism. The caves located in the gorges (Dzudzuana Cave and Bondi Cave) and along the rivers were characterised by high dampness, perhaps making their occupants more prone to malaria and rheumatism than people living in the caves located in open and dry places (Satsrublia and Kotias Klde).

In the Upper Palaeolithic, the biggest problem for the population living in cave dwellings was probably gout and callouses.

Since most herbs are ruderal, communities of the Upper Palaeolithic used for medical purposes essentially those plants that grew near their dwellings.

6. Conclusion

The study of modern spectra of cave sediments inside and outside the cave and of the role of *C. jacea* L., *A. annua* L., *A. absinthium* L., *A. millefolium* L. and *U. dioica* L. pollen showed that pollen grains of these species in the study region are not transported by wind over long distances and therefore in caves their pollen content is very low.

In the Upper Palaeolithic layers, significant amounts of *C. jacea*, *A. annua*, *A. absinthium*, *A. millefolium* and *U. dioica* pollen were recorded in the cave, likely due to their flowering branches being brought in by humans for use.

Detailed consideration of the pharmacological characteristics of the examined species showed that almost all of them have anti-inflammatory, antibacterial, antimicrobial and antipyretic activity and could be used successfully for the treatment of many inflammatory diseases.

The fossil pollen complex of medicinal herbs, dominated by *A. millefolium* and *A. annua*, suggests that the ancient population living in the studied caves could have been prone to rheumatism, malaria and gastrointestinal diseases.

In the Upper Palaeolithic, the population inhabiting cave sites might have suffered from gout and callouses.

The population of the caves located in the gorges and along the rivers and characterised by high dampness was probably more prone to malaria and rheumatism than people living in the caves located in open and dry places.

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