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Effect of Climate on Plant Growth and Level of Adaptogenic Compounds in Maral Root (*Leuzea charthamoides* (Willd.) DC.), Crowned Saw-wort (*Serratula coronata* L.) and Roseroot (*Rhodiola rosea* L.)

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ABSTRACT

Maral root (*Leuzea charthamoides* DC), roseroot (*Rhodiola rosea* L.), and crowned saw-wort (*Serratula coronata* L.) were grown in a phytotron under controlled conditions at 9, 15, 21°C day/9°C night and 21°C. All these treatments had 24 hours of light (long day-LD). In addition there was one treatment at 21°C with only 12 hours of light (short day-SD). Plants were harvested after four months and plant growth was recorded. Leaves of *S. coronata* and the underground part of *L. carthamoides* and *R. rosea* were dried and analyzed for adaptogenic compounds. The number of shoots and dry weight of caudex with roots of *R. rosea* increased by raising the temperature from 9 to 15°C. Differentiated day and night temperature with an average temperature of 15°C further increased the growth. The lowest number of shoots and the lowest dry weight of roots were produced at the highest temperature (21°C). The concentration of tyrosol and cinnamic alcohol in dried *R. rosea* roots and rhizomes was significantly affected by temperature and the highest levels were achieved at the lowest temperature, and the northernmost clone had the highest content of adaptogens at all temperatures compared to the southern clones. Growth of *L. carthamoides* leaves and underground part was the best at the two intermediate temperature treatments, while *S. coronata* seemed to prefer warmer temperatures and produced most leaves at 21°C. At 21°C, short days had negative effect on growth of all three species. The levels of ecdysteroids were significantly affected by temperature in both roots of *Leuzea* and of *Serratula* leaves with the highest levels at the intermediate (15°C) temperature.

Keywords: adaptogen, arctic plants, climatic effects
Abbreviations: 20E, 20-hydroxyecdysone; **h**, hours; **In**, 25S-inokosterone; **LD**, long day; **SD**, short day

INTRODUCTION

The species included in this project were roseroot (also called "golden root" or "Arctic root") (*Rhodiola rosea* L.), maral root (*Leuzea charthamoides* (Willd.) DC., synonymous Latin names are *Rhaponticum carthamoides* (Willd.) Iljin and *Stemmacantha charthamoides* (Willd.) M. Dittrich and crowned saw-wort (*Serratula coronata* L.). All of them are classified as adaptogenic herbs. Adaptogens were discovered in 1946 by the Russian scientist Dr. Nikolay Lazarev (Lazarev 1946). Since then more than a thousand experimental and clinical studies on adaptogens have been done, most of them in Russia and Germany. Adaptogens are defined as a class of metabolic regulators which increase the ability of an organism to adapt to environmental factors and to avoid damage from such factors (Pannosian *et al*. 1999) and the active ingredients can be divided into two groups, phenolic compounds and tetracyclic triterpenoids (Pannosian and Wikman 2005). Extracts of roots and rhizomes of *R. rosea* belong to the first group (phenolic compounds) of adaptogens and the most known are the rosavins and salidroside (Brown *et al*. 2002, 2004). Roots of *L. charthamoides* and leaves of *S. coronata* are members of the second group (tetracyclic triterpenoids) with their ecdysteroids (5 β-cholest-6-on-7-ene derivatives) (Abubakirov 1975; Dragland 1998; Volodion 2003; Budesinsky *et al*. 2008; Kokoska and Janovska 2009).

Rhodiola rosea (family *Crassulaceae*) is widely distributed in the Arctic and mountainous regions throughout Europe and Asia (Frolov and Poletaeva 1998; Khanum *et al*. 2005) and has been used in traditional medicine in Scandinavia, North-East Europe, Russia and in many countries in Asia to increase physical endurance, work productivity, longevity and as a medicine against numerous diseases such as flu, infections, headache, inflammations, depression, cancer and cardiovascular diseases (Spasov *et al*. 2000a; Tolonen *et al*. 2003; Saratikov and Krasnov 2004; Khanum *et al*. 2005). Several studies, most of them performed in earlier Soviet Union, indicate that *Rhodiola* root extracts have anti-fatigue, anti-stress, anti-hypoxic, anticancer, antioxidant, anti-inflammatory effect, immune enhancing and sexual stimulation effects (Darbinyan *et al*. 2000; Spasov *et al*. 2000b; Brown *et al*. 2002; Abidov *et al*. 2004; Brown *et al*. 2004; Saratikov and Krasnov 2005).

Leuzea carthamoides (family *Asteraceae*) is a perennial medicinal plant endemic for Siberia, Russia. It grows in the high alpine and subalpine meadows at 1200-1900 m above sea level (Dragland 1998). The plant has a woody rhizome with wiry roots with a length of 20-40 cm. The adaptogenic ecdysteroids are extracted from the roots of *Leuzea* as the content of ecdysteriods is 0.1-0.3% of the dry matter in roots, while as low as 0.01-0.1% in leaves (Syrov and Kurmukov 1976; Volodin 2003). Only 20-hydroxyecdysone is currently considered to play an important role in the adaptogenic action of *Leuzea* (Syrov and Kurmukov 1976). Harvesting is simpler with *Serratula coronata* L. (syn. *Serratula wolffii* Andrae) (family *Asteraceae*) that have high levels of several ecdysteroids in the leaves (Volodin *et al*.

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1998), where as much as 2.3% 20-hydroxyecdysone have been reported (Bàthori *et al*. 1999; Chadin *et al*. 2003). *Serratula* is a perennial plant with a widespread distribution throughout large parts of Europe and Asia (Komarov 1963). Extracts from *Leuzea* roots have been shown to have antibacterial (Kokoska *et al*. 2002; Havlik *et al*. 2009) and anticarcinogenic effects (Gaube *et al*. 2008). Phytoecdysteroids have been reported to have antidepressive effects (Ibatov 1995); they increase protein synthesis (Syrov and Kurmukov 1976), improve physical and sexual performance and prevent infections (Gadzhieva *et al*. 1995; Azizov *et al*. 1997; Mirzaev *et al*. 2000).

Presently there is an increasing demand for herbs grown in the Northern regions because of assumed better quality (higher content of active compounds), and the added marketing value herbs from the arctic can represent. Domestic production of herbs and medicinal plants can also be a new alternative income for farmers, in addition to the traditional agricultural production. The results of several cultivation experiments have been published by Galambosi *et al*. (2003) and Dragland (1998, 2004). Nevertheless, there are still unsettled problems preventing them from being widely cultivated. These problems arise due to the exhaustion of the supply of wild plants, lack of cultivation techniques and large variation of active compounds.

All species in this study have good climatic tolerance and represents potential new cultures for growers in the Arctic regions. Northern growing conditions are characterized by long days with ample light and relatively low temperatures during the growing season. The light intensity, photoperiod and temperature have been reported to influence the biosynthesis of many secondary metabolites (Hohtola 2007; Bidart-Bouzat and Imeh-Nathaniel 2008; Bruni and Sacchetti 2009). The explanation is that secondary metabolites mainly act as defence substances in plants subjected to stress (Shain 2005; Hohtola 2007). In this study, performed under controlled climatic conditions, we tested the hypothesis that low temperatures and long days increase the level of adaptogenic compounds, and that plants from northern areas have adapted to northern growing conditions during evolution by producing higher levels of secondary metabolites of adaptogenic nature than clones/plantlets from the same species with a more southern origin.

MATERIALS AND METHODS

Plant material

The *R. rosea* plants were clonal material originated from Buren close to Tromsø, Northern Norway (69° 39′ N, 18°57′E), Kise, South-East Norway (60° 77′ N, 10° 80′ E) and from Rovaniemi, North Finland (66° 30′ N, 25° 44′ E). The Tromsø material all originated from the same clone while the Kise and Rovaniemi plants originated from two and six individual clones, respectively. The *L. chartamoides* individuals used in the experiment was from one single seed population (origin from Mikkili, Finland, 61° 41′ N, 27° 16′ E) and 6 years old clonally propagated plants from two different clones, these also with origin from Mikkili. The seedlings of *L. carthamoides* were four months old. *S. coronata* plants were all one year (150 plants) and four months (50 plants) old and originated from one single seed population from Syktyvkar, Komi, Russia (61° 40′ N, 50° 48′ E). The initial origin of plants was from Western Siberia.

Experimental design

In order to study climatic and genetic effects of the climate on growth and level of adaptogenic compounds, plants were grown at the following temperature treatments; 1) 9°C, 24 h light (LD); 2) 15°C, 24 h light; 3) 21°C during daytime and 9°C during night, 24 h light; 4) 21°C, 24 h light and 5) 21°C, 12 h light (SD). Daylight was supplemented with cool white fluorescent tubes giving the minimum of 150 μmol cm^{-2} s^{-1} PAR, and plants at 12 h light were placed in a dark growth room at the respective treatments from 20:00 to 08:00. The humidity was regulated to ensure 0.5 MPa water vapor deficits. Plants were watered daily, and fertilized with a complete nutrient solution once a week. The experiment took place from the Aug 31 to Nov 9, 2007. Each treatment had 28, 36 and 40 individuals of *R. rosea*, *L. carthamoides* and *S. coronata*, repectively. The different genetic materials of each species were divided equally among the different treatments.

Chemical analysis

After 15 weeks growing plant material (leaves of *S. coronata* and underground part of *R. rosea* and *L. carthamoides*) was harvested, washed, sliced and dried at 40°C for 10 days. All soil was removed from the roots by washing. The *R. rosea* samples were quantified for salidroside, rosavin, total rosavins, tyrosol and cinamic alcohol per HPLC by PHARMAPLANT Medicinal and Aromatic Plants Research and Breeding, Ltd. Germany, a DIN EN ISO 9001:2000 accredited laboratory. About 20 g (dry weight) of each sample were grounded, and of this 15 g powder of each sample were extracted with 25 ml of 96% EtOH in a shaker (150 rpm) for 24 h at room temperature. After filtration, the filtrate was dried in a rotavapor at room temperature and redissolved in 10 ml 50% EtOH. The ethanol extracts were analysed with validated HPLC methodology, with inter-and intraday precision and accuracy well within internationally accepted values (CV < 15%) (Hellum *et al*. 2009). The analysis of ecdysteroids was performed as described by Chadin *et al*. (2003b) on dry leaf (*S. coronata*) and root material (*L. carthamoides*).

Statistics

Statistical analysis of growth data, flower development and adaptogens were performed using the General Linear Model procedure of Minitab 15. Data from *S. coronata* was analysed for effects of plant origin, temperature treatment and interaction between origin and treatment. For *R. rosea* and *L. carthamoides* the analysis in addition included effects of clone (nested within plant origin) and interaction between clone and temperature treatment.

RESULTS AND DISCUSSION

The growth of the plants was very much affected by the temperature treatments (**Fig. 1, Tables 1-3**). Short days at 21°C severely decreased the growth of all three species. They inhibited production of flowers completely in *S. coronata* and *L. carthamoides* while LD treatment at the same temperature gave 2.0 and 1.3 flowers per plant for *S. coronata* and *L. carthamoides*, respectively. The negative effect of SD on growth and flower development reflect the fact that these plants are adapted to northern conditions with long days during the growth season.

The best growth of golden root (*R. rosea*) at the LD

Table 1 Climatic effects on growth and level in adaptogenic compounds of *Rhodiola rosea*.

Treatment °C	Number of shoots	Root dry weight (g)	Cinnamic alcohol mg/g d.w.	Rosavin mg/g d.w.	Tyrosol mg/g d.w.	Salidroside mg/g d.w.	Total rosavines mg/g d.w
	P=0.000	P=0.020	P=0.001	P=0.371	P=0.000	P=0.311	P=0.180
9	28.3	17.6	0.75	3.02	0.15	2.42	5.59
15	30.3	21.9	0.67	2.98	0.11	3.34	4.96
21/9	40.3	24.1	0.72	2.66	0.09	2.85	4.66
21, SD	12.3	13.2	0.61	3.29	0.06	3.27	4.97
21, LD	22.5	15.4	0.66	2.94	0.06	2.98	4.75

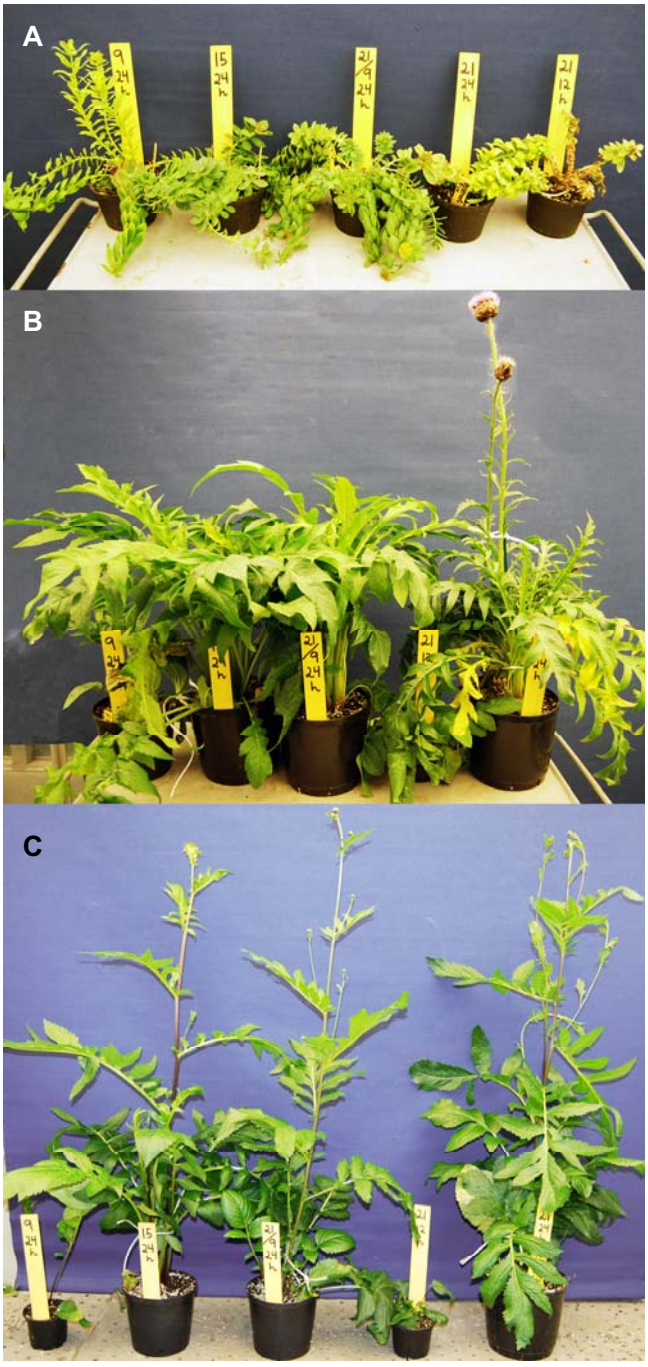

Fig. 1 Representative individuals of (**A**) *Rhodiola rosea*, (**B**) *Leuzea chartamoides* and (**C**) *Serratula coronata* after 3 months at (from left to right) 9°C, 24 h light (LD); 15°C, 24 h light; 21°C during daytime and 9°C during night, 24 h light; 21°C, 24 h light and 21°C, 12 h. Photos: Gunnlaug Røthe and Inger Martinussen.

Table 2 Climatic effects on growth and level of the ecdysteroid 20-hydroxyecdyzone (C 20E) in *Leuzea chartamoides*.

Treatment °C	Height (cm)	Flowers	Root dry weight (g)	C 20E %
	P=0.000	P=0.000	P=0.000	P=0.000
9	53.0	0	1.7	0.05
15	68.5	0.4	5.5	0.14
21/9	69.8	0.5	4.2	0.14
21, SD	30.2	0	1.4	0.11
21, LD	59.7	1.3	2.4	0.06

Table 3 Climatic effects on growth and level of ecdysteroids 20-hydroxyecdyzone (C 20E) and 25S-inokosterone (IN) in *Serratula coronata*.

Treatment °C	Height (cm)	Number of flowers	Leaf dry weight (g)	C 20E %	In %
	P=0.000	P=0.000	P=0.000	P=0.000	P=0.001
9	20.3	0	0.8	0.13	0.09
15	93.1	1.4	11.4	0.30	0.42
21/9	80.0	2.9	8.2	0.27	0.23
21, SD	17.2	0	0.9	0.10	0.06
21, LD	81.8	2.0	16.0	0.27	0.13

treatments was at the differentiated day and night treatment (21°C at day, 9°C at night = average temperature 15°C) while number of shoots and dry weight of roots was lowest at 21°C. However, the different clones from different geographical origins differed considerably in their response to the temperature treatment. Number of clones for each geographical origin was 1, 6 and 2 for Buren, Rovaniemi and Kise, respectively. There were a significant effect of origin on number of shoots (p=0.000) and dry weight of roots (p=0.000) and there was a significant interaction between geographical origin and treatment on both shoots (p=0.000) and roots (p=0.006). Number of shoots were significantly affected by clone (p=0.000), while dry weight of roots was not (p=0.913). The interaction between clone and treatment was not significant on either shoot or root production. The growth of the single northernmost clone from Buren, Tromsø, was not significantly affected by the temperature treatments. There were no variation in root growth between the six different clones from Rovaniemi, however, clone R3 produced far more shots than the others at 21/9 and 9°C (**Fig. 2A**). The biggest plants in this experiment were the two southernmost clones from Kise, South-East Norway. Interestingly, the growth of the southernmost material was affected by the temperature treatment with a severe reduction in growth (number of shoots) at the SD treatment. This is reflected in the results of all clones together given in **Table 1**. The Kise plants have been growing at Kise for years but are originally from Hofstad in Mid Norway (64° 11′ 48″ N, 10° 24′ 09″ E). This can explain the adaptation to long days.

The maral root (*L. chartamoides*) plants had two origins; one seed population from Mikkili and two different clones from Mikkili. There was a significant difference between the two different origin of plants (clonal or seed plants) on both plant height (p=0.000) and root weight (p=0.000), but no difference within the clonal material and within the seed population. This can be explained by a different age of the plant material, as the seed plants were only three months old while the clonal plants originated from six-year-old mother plants. The best growth (height and root weight) of *L. carthamoides* was at the two intermediate temperature treatments (21/9 and 15°C, both LD) (**Fig. 1B, Table 2**). On the contrary the low temperature treatment (9°C LD) and the SD treatment given at 21°C gave the lowest plants and smallest roots. The effect of treatments was significant for all growth parameters measured.

The *S. coronata* plants all originated from one seed population; however, there were two different age classes. The reason for this was problems with germination after the first sawing of seeds. The two groups of plants differed by one year in age and this was reflected on the growth as there was a significant difference between the two groups on both plant height (p=0.000) and dry weight of leaves (p=0.016). The *S. coronata* plants grow poorly and produced no flowers at the lowest temperature and at 21°C when given short days (**Fig. 1, Table 3**). There was a significant difference in height between the above mentioned treatments and the others. The highest production of leaves were at the highest temperature (p=0.000) at long days.

The concentration of tyrosol and cinnamic alcohol in *R. rosea* roots was significantly affected by temperature (**Table 1**) and the levels were highest at the lowest temperature. The other adaptogenic compounds in *R. rosea* tended to be higher at the lowest temperatures (9 and 15°C) than at 21°C, but the results were not significant. The northernmost clone of *Rhodiola* (Buren) had interestingly the highest

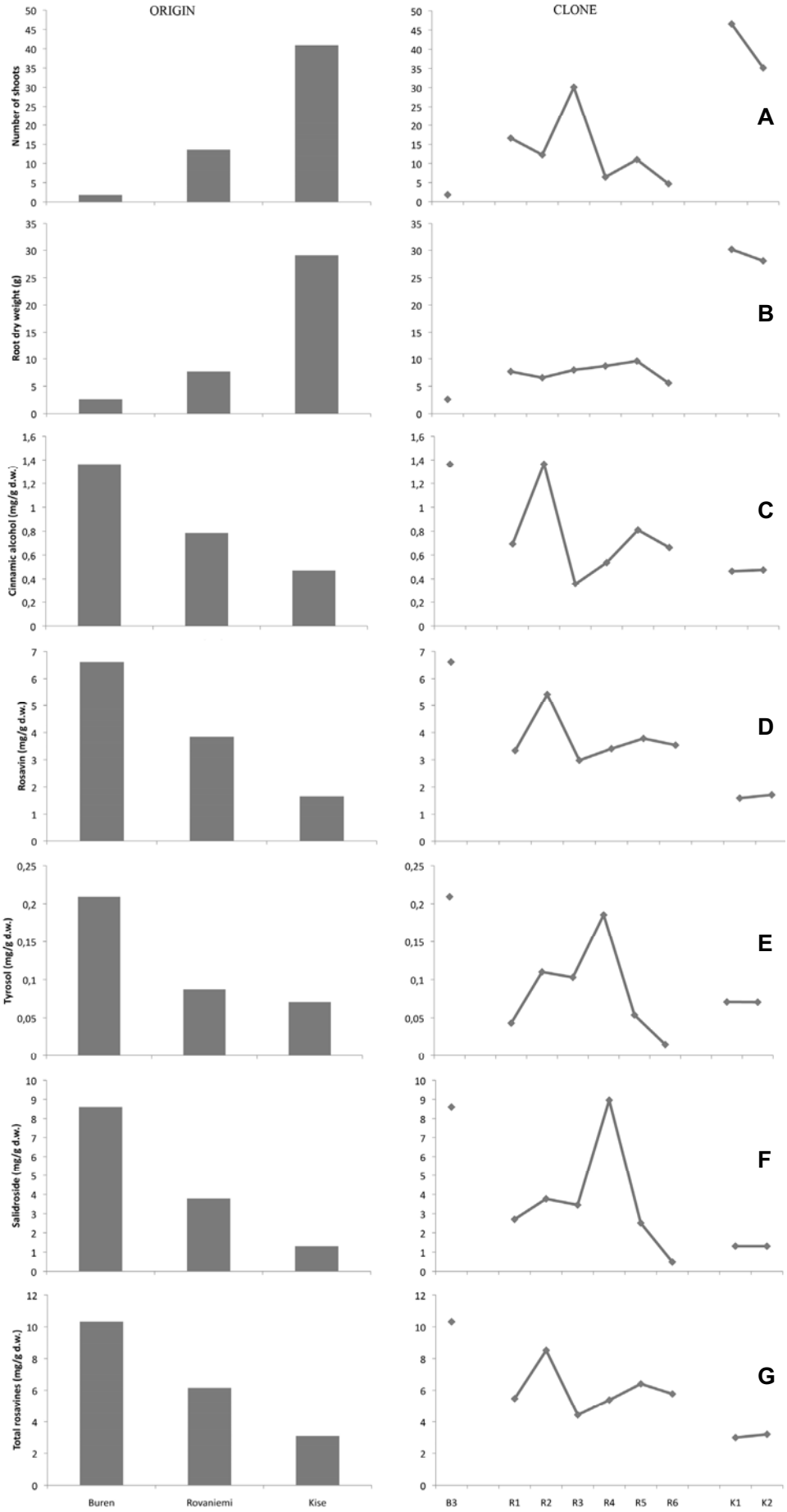

Fig. 2 Measured growth parameters and levels of adaptogens in the *Rhodiola* material from 3 different geographical origins; Buren, Northern Norway; Rovaniemi, North Finland and Kise, South-East Norway. The mean values for the geographical origins are shown to the left while the variation between each clone is shown to the right. (**A**) Number of shoots; (**B**) Dry weight of roots; (**C**) Concentration of cinnamic alcohol (mg/g dry weight) in the roots (**D**); Concentration of rosavin in the roots; (**E**) concentration of tyrosol in the roots; (**F**) Concentration of salidroside in the roots; (**G**) Concentration of total rosavines in the roots.

content of all adaptogens at all temperature treatments compared to the clones from the more southern origins (Rovanimi and Kise) (**Table 1**), and there was a significant interaction between geographical origin and treatment for both the content of tyrosol (p=0.009) and cinnamic alcohol (p=0.000). Galambosi *et al*. (2007) compared levels of phenylpropanoids in roseroot clones collected from wild populations in North Finland with levels in clones cultivated in South Finland and found that clones from the north (Kilpisjärvi) had the highest levels of total rosavins and salidroside, however, plant age, temperature, soil, etc. differ and it is hard to conclude anything about both genetic effects and effect of a northern climate. It should be taken into consideration that the northernmost origin in this study is represented by only one single clone while Rovaniemi and Kise is represented by six and two clones, respectively. The six clones from Rovaniemi are considerably different in content of the different adaptogens with R4 high in tyrosol and salidroside (**Figs. 2E, 2F**) and R2 high in rosavin, total rosavines and cinnamic alcohol (**Figs. 2D, 2E, 2G**). These levels are almost similar to the levels of the northernmost clone (Buren). However, Buren is the only clone that had a high level (and higher than the others) of all analysed adaptogens. In an experiment performed on *R. rosea* clones collected from 15 different counties in Norway, from Finnmark in the North to "Vest- and Aust-Agder" in the South, Dragland and Mordal (2006) found large variations in both rosavin and salidroside contents between and within the counties. There was no clear pattern in level of adaptogens in relation to origin, and the levels in northern clones were not higher than in clones from the south. This experiment was performed on 6-8 clonally propagated plants each of a total of 93 clones in one field with uniform growth conditions. The number of locations from each county varied considerably (from 18 to one), and the environment was not controlled. In a separate study (Hellum *et al*. 2009), using six of the same clones as described by Dragland and Mordal (2006), found a large variation in active constituents between the clones, unfortunately the origin of the different clones is not given. Interestingly, the variation in active constituents seemed to be of minor importance to the inhibition of CYP3A4 and P-gp.

The concentration of analyzed ecdysteroids was significantly affected by temperature in both *L. carthamoides* roots with rhizomes and *S. coronata* leaves. The levels of both 20-hydroxyecdysone (20E) and 25S-inokosterone (In) was highest in leaves from *S. coronata* plants grown at 15°C and the differentiated day night treatment 21/9°C (mean temperature 15°C) and lowest at the SD treatment and at 9°C. In *L. carthamoides* leaves, highest concentration of 20E in roots was at 15°C. In *L. carthamoides* leaves the highest level of 20E in roots with rhizomes was gained at 15°C, but the SD treatment at 21°C did not have any negative effect compared to the LD treatment at the same temperature. Levels of 20E were 0.11% at SD and 0.06% at LD. The two age classes of *S. coronata* seedling did not differ in content of ecdysteroids, and similar for the two different clones of *L. carthamoides* from Mikkili.

CONCLUSIONS

The conclusion is that all three herbs species included in this study are very well suited to be cultivated at northern conditions. The results indicate that it might be an advantage to grow *R. rosea* and *L. carthamoides* at low average temperatures, while *S. coronata* should be grown at slightly warmer places, however, it must be remembered that the experiment is limited to a restricted genetic material of each species. The results with *R. rosea* indicate that clones from the north might have a higher content of adaptogens than clones from more southern areas, while levels of ecdysteroids in *L. carthamoides* and *S. coronata* were highest at medium temperature (15°C). The presented results are valuable in order to choose the best plant material for cultivation at different geographic origins.

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REFERENCES

Abidov M, Grachev S, Seifulla RD, Ziegenfuss TN (2004) Extract of *Rhodiola rosea* radix reduces the level of c-reactive protein and creatinine kinase in the blood. *Bulletin of Experimental Biology and Medicine* **7**, 63-64

Abubakirov NK (1975) Edysones – insect hormones. *Chemistry and Life* **11**, 57-62 (in Russian)

Azizov AP, Seifulla RD, Chubarova AV (1997) Effects of *Leuzea* tincture and leveton on humoral immunity of athletes. *Eksperimentalnania i Klinicheskaia Farmakologiia* **60**, 47-48

Bàthori M, Kalàsz H, Csikkelnè SA, Màthè I (1999) Components of *Serratula* species; screening for ecdysteroid and inorganic constituents of some *Serratula* plants. *Acta Pharmaceutica Hungaria* **69**, 72-76

Bidart-Bouzat MG, Imeh-Nathaniel A (2008) Global change effects on plant chemical defenses against insect herbivores. *Journal of Integrative Plant Biology* **50**, 1339-1354

Brown RP, Gerbarg PL, Ramazanov Z (2002) *Rhodiola rosea*: A phytomedicinal overview. Herbal gram. *Journal of the American Botanical Council* **56**, 40-52

Brown RP, Gerbarg PL (2004) The *Rhodiola* Revolution. Transform Your Health with the Herbal Breakthrough of the 21st Century. Rodale Books, City, 260 pp

Bruni R, Sacchetti G (2009) Factors affecting polyphenol biosynthesis in wild and field grown St. John's Wort (*Hypericum perforatum* L. *Hypericaceae*/*Guttiferae*). *Molecules* **14**, 682-725

Budesinsky M, Vokàc K, Harmatha J, Cvacka J (2008) Additional minor ecdysteroid components of *Leuzea carthamoides*. *Steroids* **73**, 502-514

Chadin I, Kolegova N, Volodin V (2003a) Distribution of 20-hydroxyecdysone on generative plants of *Serratula coronata* L. *Siberian Ecological Journal* **1**, 49-53

Chadin I, Volodin V, Whiting P, Shirshova T, Kolegova N, Dinan L (2003b) Ecdysteroid content and distribution in plants of genus *Potamogeton*. *Biochemical Systematics and Ecology* **31**, 407-415

Darbinyan V, Kteyan A, Panossian A, Gabrielian E, Wikman G, Wagner H (2000) *Rhodiola rosea* in stress induced fatigue: a double blind cross-over study of a standardized extract SHR-5 with a repeated low-dose regimen on the mental performance of healthy physicians during night duty. *Phytomedicine* **7**, 365-371

Dragland S (1998) REINROT – en ny plante med mange muligheter. *Grønn forskning* **03/98**, 36 pp (in Norwegian)

Dragland S (2004) Roseroot (*Rhodiola rosea*) – status and future in Norwegian agriculture. *Grønn Kunnskap* **8**, 291-294

Dragland S, Mordal R (2006) Variasjoner i rosenrot (*Rhodiola rosea*) fra 97 steder i Norge. *Bioforsk TEMA* **1**, 1-4 (in Norwegian)

Frolov Yu, Poletaeva I (1998) *Rhodiola rosea* in the European North-East. UrD RAS Ekaterinburg, 192 pp (in Russian)

Gadzhieva RM, Portugalov SN, Paniushkin VV, Kondrat'eva II (1995) A comparative study of the anabolic action of ecdysten, leveton and prime Plus, preparations of plant origin. *Eksperimentalnania i Klinicheskaia Farmakologiia* **58**, 46-48

Galambosi B, Galambosi Zs, Valo R, Kantanen S, Kirjonen H (2003) Elaboration of cultivation methods for roseroot (*Rhodiola rosea* L.) in Mikkeli, 1994-2002. In: Galambosi B (Ed) Use and introduction of medicinal plants with adaptogen effects in Finland. *Maa- ja elintarviketalous* **37**, 47-62. Available online: www.mtt.fi/met/pdf/met37.pdf

Galambosi G, Galambosi Zs, Slacanin I (2007) Comparison of natural and cultivated roseroot (*Rhodiola rosea* L.) roots in Finland. *Zeitschrift für Arznei- and Gewürzpflanzen* **12**, 141-147

Gaube F, Wölfl S, Pusch L, Werner U, Kroll TC, Schrenk D, Hartmann RW, Hamburger M (2008) Effect of *Leuzea carthamoides* on human breast adenocarcinoma MCF-7 cells determined by gene expression profiling and functional assays. *Planta Medica* **74**, 1701-1708

Havlik J, Budesinsky M, Kloucek P, Kokoska L, Valterova I, Vasickova S, Zeleny V (2009) Norsesquiterpene hydrocarbon, chemical composition and antimicrobial activity of *Rhaponticum carthamoides* root essential oil. *Phytochemistry* **70**, 414-418

Hellum BH, Tosse A, Hoybakk K, Thomsen M, Rohloff J, Nilsen OG (2009) Potent *in vitro* inhibition of CYP3A4 and P-glycoprotein by *Rhodiola rosea*. *Planta Medica* **75**, 1-8

Hohtola A (2007) Northern plants as a source of bioactive products. In: Taulavuori E, Taulavouri K (Eds) *Physiology of Northern Plants under Changing Environment*, Old City Publisher, Philadelphia, USA, pp 291-307

Ibatov AN (1995) The use of a decoction of the rhizome of *Leuzea cartha-*

moides for the treatment of alcoholics with depressive states. *Zhurnal nevrologii i psikhiatrii imeni S.S. Korsakova* **95**, 78-79

Khanum F, Bawa AS, Singh B (2005) *Rhodiola rosea*: A versatile adaptogen. *Comprehensive Reviews in Food Science and Food Safety* **4**, 55-62

Kokoska L, Polesny Z, Rada V, Nepovim A, Vanek T (2002) Screening of some Siberian medicinal plants for antimicrobial activity. *Journal of Ethnopharmacology* **82**, 51-53

Kokoska L, Janovska D (2009) Chemistry and pharmacology of *Rhaponticum carthamoides*: A review. *Phytochemistry* **70**, 842-855

Lazarev NV (1946) Experimental data for the evaluation of the Far East Schizandra as a stimulant. In: *Proceedings of the scientific medical board at the administration of medical-sanitary department of the USSR navy Issue 1*. **5**, 62-69. Leningrad: Military Press of the Ministry of Armed Forces of USSR

Mirzaev IR, Syrov VN, Khrushev SA, Iskanderova SD (2000) Effect of ecdystene on parameters of the sexual function under experimental and clinical conditions. *Eksperimentalnania i Klinicheskaia Farmakologiia* **63**, 35-37

Panossian A, Oganessian A, Ambartsumian M, Gabrielian E, Wagner H, Wikman G (1999) Effects of heavy physical exercise and adaptogens on nitric oxide content in human salvia. *Phytomedicine* **6**, 17-26

Panossian A, Wikman G (2005) Effect of adaptogens on the central nervous system. *Arquivos Brasileiros de Fitomedicina Cientifica* **3**, 29-51

Saratikov A, Krasnov E (2004) *Rhodiola rosea* (golden root). Tomsk University, 290 pp (in Russian)

Shain S (2005) *Bioregulation of Plant Productivity*, Overley, Moscow, 228 pp (in Russian)

Spasov AA, Mandrikov VB, Mironova IA (2000a) The effect of the preparation rodiosin on the psychophysiological and physical adaptation of students to an academic load. *Eksperimentalnania i Klinicheskaia Farmakologiia* **63**, 76-78

Spasov AA, Wikman GK, Mandrikov VB, Mironova IA, Neumoin VV (2000b) A double-blind, placebo-controlled pilot study of the stimulating and adaptogenic effect of *Rhodiola rosea* SHR-5 extract on the fatigue of student caused by stress during an examination period with a repeated low-dose regimen. *Phytomedicine* **7**, 85-89

Syrov VN, Kurmukov AG (1976) On the anabolic activity of phytoecdysone – ecdysterone extracted from *Rhaponticum carthamoides* (Willd.) Iljin. *Farmakologiya i Toksikologiya* **39**, 690-693

Tolonen A, Hohtola A, Jalonen J (2003) Comparison of electrospray ionization techniques in the analysis of the main constituents from *Rhodiola rosea* extracts by liquid chromatography/mass spectroscopy. *Journal of Mass Spectrometry* **38**, 845-853

Volodin VV (2003) *Phytoecdysteroids*, Nauka, St. Petersburg, 293 pp

Volodin VV, Alexeeva LI, Kolegova NA, Sarker SD, Šik V, Lafont R, Dinan L (1998) Further ecdysteroids from *Serratula coronata* L. (*Asteraceae*). *Biochemical Systematics and Ecology* **26**, 459-461