REVIEW ARTICLE

THE INFLUENCE OF CLIMATE ON THE ACTIVE PRINCIPLES IN MEDICINAL PLANTS

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INTRODUCTION

THE content of active principles in living medicinal plants is the balance between their formation and their elimination during growth. Formation and elimination are effected by two main groups of factors: the first group is comprised of those which are based on hereditary properties of the plant and therefore fixed, and the second group those which are based on external influences, called the ecological or environmental or phenotypical effects, the main sources being the soil, the climate, the neighbouring plants and, as far as the plant is cultivated, the procedures of this cultivation. In a previous review the writer[1] has dealt with the influence of soil on active principles and it is now proposed to consider the influences of the climate.

There exist some hundreds of publications on the subject, and these fall into two more or less distinct groups, at least until the years around 1940. The more numerous group is concerned especially with the yield of active principles in the course of production of drugs having a high content of active principles. Here, work has been performed mostly by pharmacognosists and drug producers with scientific interest. The other less numerous group deals with the formation and elimination of the active principles as physiological processes, and the investigations of this group originate mostly from plant physiologists. The authors of the first group have often extended the interpretation of their results to physiological problems, but this is acceptable only if the necessary care had been taken in performing the investigation, such as the use of a physiologically reliable reference base[2], consideration of all possible sources of error, etc.

It is striking that in books dealing with ecology (reaction of plants to environmental influences) the active principles of medicinal plants are given very little attention. For instance Lundegardh[3] in the fourth edition of his famous and excellent book "Klima and Boden in ihrer Wirkung auf das Pflanzenleben" scarcely deals with the active principles of medicinal plants; only the main physiological processes (assimilation, respiration, growth, etc.) are discussed. Also Paech[4] in his valuable and useful book on the biochemistry and physiology of secondary plant products mentions only a few results on the influences of ecological factors on the formation of these products.

General Considerations

As mentioned in the writer's former review[1], contradictory results can be found in various investigations on the same subject. Reference should be made to that discussion and to a general discussion of the subject by Hegnauer[5]. The main reasons for these contradictory findings are briefly enumerated and to them are added others which are especially important in investigations of the influence of the climate.

1. The values obtained by most of the assay-methods are not absolute, and the methods employed should always be indicated. In this connection a proposal of Hegnauer[5] may be briefly discussed. He proposes to use the "glandular hair index" (proportion of glandular hairs to total epidermal cells), on species with glandular hairs, as a measure of their capacity to produce essential oils. As can easily be appreciated, the index or also the number of glandular hairs per leaf indicate the number or the density of possible loci for the formation of the active principles. It is, however, highly probable that within a linnean species the production in these loci will also differ according to hereditary properties. Therefore the quantity of active principles synthesised and the content may differ in organs with the same index of glandular hairs or of other loci of formation.

2. Due consideration must be given to statistical requirements (limits of error, sufficient repetition, interpretation, etc.) and these statistics should be noted in the publication.

3. The diurnal, seasonal and other similar variations of the content of active principles are often greater than the variation to be studied. Care should therefore be taken to harvest all series when the physiological conditions of the plants are the same and records of this condition must be given. Hegnauer[5] has proposed to determine the moment of harvest not by externally recognisable characters (flowering, fruiting, etc.) but by the aid of the ratio of special components of the plant, e.g., the ratio of menthone to menthol. The writer believes that this would be only admissible for pure strains, because in genetically heterogeneous plant material such a ratio may vary considerably and perhaps independently of other processes.

4. The reference base should be a suitable one for the investigation. Dry weight has its own seasonal and diurnal variation and is therefore not suitable for physiological investigations. It is, on the other hand, the most suitable reference base for the grower, the buyer and the user. For physiological purposes fresh weight, surface area of the organ (for leaves, etc.) crude fibre, calcium, number of plants or organs, etc., are suitable reference bases depending on the aim of the investigation.

5. The plants should be genetically as uniform as possible (pure strains, clones (vegetative propagants of one mother plant), seeds from one mother plant or of a selected race, etc. Unfortunately such genetically uniform strains are still not available for most of the species of medicinal plants.

6. Ecological factors may in a certain measure replace one another and they will often influence one another[6], e.g., wind may have a drying

effect like that of reduced humidity. In spite of a sufficient supply of water, plants may then wilt as in a dry climate. Therefore all climatic factors at the moment of the investigation should be recorded as far as possible.

7. It is not sufficient to determine only two points of a variable factor, e.g., extremely dry and extremely humid, one high and one low altitude, etc., since the results could be random ones and give no information about how the plants behave in the range between the two determined points. Therefore for the comparison of the influence of an ecological factor, the responses to different grades must be determined. If only two points are determined general conclusions should be avoided.

Distribution of the Chemical Groups of Active Principles Throughout the Climatic Regions

In textbooks and manuals on medicinal plants sometimes vague indications are given about the distribution of the different chemical groups of active principles in the various climatic belts of the world but very few critical examinations have been published.

McNair[7] in a careful study has examined the ratio of alkaloid-bearing families to the total families in the tropics and in temperate regions and found that in the former three times as many alkaloidal families exist as in the latter. However, the ratio of alkaloidal families to total families is nearly the same in both zones, the greater variation of species and families being the reason for the greater abundance of alkaloids in the tropics. Webb[8] compared the number of alkaloidal species and their ratio to total species in different ecological formations of Australia and found that the tropical rain forest contains the highest proportion and the hot and arid zones the lowest proportions of alkaloidal species. Here again the total number of species (100 in the arid zone and the 400 to 500 in the tropical forest with 5 to 10 per cent. of alkaloidal species) must be considered. Also to be noted is the fact that in the arid zone, families without or with very few alkaloidal species (Myrtaceæ, Proteaceæ, Gramineæ) prevail whilst in the rain forest many typical alkaloidal families are present. Among alkaloidal families growing in both formations are Rutaceæ, Leguminosæ and Liliaceæ. None of their representatives in the arid zone contain alkaloids whilst many in the rain forest do so. The reasons why the ratio of alkaloidal species is apparently higher in the rain forest are still uncertain. Webb[8] points out that one reason may be that the soils in the arid zone are very poor in nitrogen (maximum 0·053 per cent.) while the soils in the rain forest are rich in that element (up to 0·61 per cent.). This condition has probably had an influence on the selection of the families and species that have become established in the two regions, and as alkaloids contain nitrogen and are produced in the course of nitrogen metabolism the distribution of alkaloidal species can thus be partly understood. Further investigations of this kind would be valuable.

Plants containing essential oils appear to be more abundant in xerophytic habitats than in mesophytic (humid) ones[9], especially as far as the Labiatæ, Umbelliferæ, Rutaceæ, Guttiferæ and Compositæ are concerned.

In mesophytic regions the total number of species is greater but those containing essential oils is smaller. A reason for this distribution may be found in the fact that in an atmosphere containing essential oils the transpiration is lower than in an atmosphere without essential oils, as had been shown by Theodoresco[10] and recently confirmed by a very skillful investigation of Heilbronn[11]. It had first been believed that the essential oil atmosphere would absorb the heat. Theodoresco[10] demonstrated that the degree of absorption is too small and Heilbronn[11] showed that the essential oils form a film by which the vapour tension is lowered. This phenomenon may have favoured species in zones with arid climates. Rovesti[12,13] in discussing the lowering of transpiration by essential oils probably gives a wrong interpretation, because he suggests that a lowering of the osmotic pressure takes place instead of the rate of transpiration. However, he also stresses that essential oils allow a species to grow in a dry habitat and furthermore he has found that the composition of the oil varies in the vapour tension of its constituents and the degree of dryness of the habitat (see under geographical races).

It has been pointed out that species with mucilage are also more abundant in dry regions. This theory must in the first instance be restricted to those species which contain the mucilage in the tissues of the vegetative organs and not in the seed coat because in the seed coat the mucilage plays a role during germination, whilst in the vegetative tissues the retaining capacity for water of these substances may help the species to live in arid climates. It must, however, also be taken into account that plant mucilages can also serve as a supply of carbohydrates[13].

No similar conclusions are available for plants containing glycosides. This is understandable because the structures of aglycones differ widely. Also glycosides are widely distributed in the majority of angiosperm families.

Summarizing the small quantity of exact knowledge about the distribution of the chemical groups of active principles over the different climatic regions of the world it can be said that, at least for several of the groups, relations between climatic conditions and ratio of species bearing special chemical groups exist, but that the distribution is mostly the result of the selection, in which the species with special chemical groups such as essential oils or mucilages are more resistant to extreme climatic conditions. It should also be noted that in such a selection various other properties and constituents may be more decisive than the concentration of the active principles.

Reactions of the Content of Active Principles to Individual Climatic Factors

Active principles may respond to climatic factors both qualitatively and quantitatively. A qualitative reaction means that the whole complex (active principles are nearly always mixtures of related substances) or one or several of its components are no longer produced if the intensity of the climatic factor is lower or higher than a certain threshold value. It must be said that this qualitative reaction has not been established with certainty up to the present, although in a recent and well done investigation[15] it is indicated that in the roots of cinchona plants grown to only 30 per cent. of full height no quinine at all was found. Such findings depend on the precision of the analytical method employed and so they cannot be considered as absolute. Theoretically lack of formation of a chemical substance, resulting from too low or a too high an intensity of a climatic factor is possible, because it also occurs during the seasonal variations of the content of active principles, e.g., with solanaceous alkaloids, where hyoscine may cease to be produced in fully mature *Datura stramonium*. The fact that a plant ceases to produce an active principle when still in a state of development in which continued production might be anticipated may possibly be explained by the "law of the minimum" which governs many metabolic processes. In this context it may be mentioned that, based on experimental findings, Paech[16] considers essential oils not as indispensable side products of metabolic processes but rather as being formed when more of the intermediate products of the carbohydrate metabolism are produced than are necessary.

Therefore, the main metabolic processes could still continue after the above mentioned surplus of intermediate substances is no longer available. It must, however, be noted that this possibility has still to be proved experimentally.

Graphs of the percentage content (and the synthesis) of active principles with reference to increasing intensity of one climatic factor (e.g., temperature or light of a determined wavelength) will probably show one peak which may be situated symetrically or asymmetrically. However, as soon as more than one climatic factor is involved, several peaks may occur and therefore, due to the interaction of the factors, the curve may become irregular.

Reference to the publications on the influence of climate on active principles shows that the required use of a pure strain or even of a clone has very seldom been fulfilled. This again will explain irregularities of curves obtained.

The investigations may be divided into several groups: (1) investigations dealing with one climatic factor (radiation, temperature, water and humidity, wind); (2) investigations dealing with special types of climates (southern, northern, high or low altitudes, arid, humid, oceanic, continental, etc.). Another subdivision may be made to separate investigations performed in laboratories from those which have been carried out on open land. Holding an intermediate position in this classification will be investigations in which, by exchange of soils or by cultivation of strains of different climatic origin in one place, the investigator has tried to eliminate as far as possible factors other than climatic ones; in this article, most of the publications relate to work that has been performed on open land. Later the problem of climatic strains of medicinal plants will be discussed.

One point will be briefly discussed before entering into the special problems. It has been stated that the formation of active principles occurs predominantly in the periods of vigorous growth or other intensive metabolic processes in the plant (e.g., flowering or fruiting) and that therefore the percentage content is highest during or immediately after such periods[17,18]. Paech[16] has recently shown that for essential oils in *Asarum europæm* a second period of oil production may occur after completion of the growth of the cell, provided that the temperature is favourable. Nevertheless Paech also found that the formation of active principles is predominantly connected with periods of intensive growth. It can therefore be expected that climatic conditions which allow a healthy and strong growth will, generally speaking, produce medicinal plants with a high content of active principles, whilst poor conditions would rather have the opposite effect.

Light (Radiation) and Active Principles

Here, only radiations with wavelengths of visible light and the neighbouring ranges (ultra-violet and infra-red) will be considered. Most of the publications deal with sunlight and only a very few are concerned with screened, narrow ranges of light radiation. The effect of light is, of course, closely connected with that of temperature, and transitions between the two ranges of radiation will often be the case as well as a certain replaceability between light and temperature.

With regard to wavelength and the chemical activity of plants, Lundegardh[3] (p. 50) in reviewing several papers states that the whole light spectrum may act as source of energy, the maximal effects being produced by the long wave range (6000 Å to 7500 Å). Side-optima may occur at ranges around 4400 Å. Formation of chlorophyll is more induced by red light and formation of carotinoids by blue light[19,20]. With regard to growth (considering the relation between growth and formation of active principles) light with wavelengths shorter than 6000 Å prevents or at least reduces growth of the cells and only longer wavelengths may stimulate growth[21,22]. The growth-retarding action of ultra-violet light can easily be seen on the smaller size and height of alpine plants, a fact which had been widely studied by Bonnier[23] and other workers.

Braun[24] found that ultra-violet light (around 3650 Å) had no effect on the oil-content of linseed; with *Datura stramonium* an irradiation of only 30 minutes increased the alkaloidal percentage from 0·1 per cent. to 0·25 per cent., whilst in *Thymus vulgaris* and *Mentha crispa* the content of essential oil, and in *Digitalis purpurea* the glycosides, were considerably reduced (digitalis 43 per cent.). These findings should be verified by further investigations.

James[25] states that for alkaloids which are produced in roots, light cannot have a direct influence on their formation. This does not mean that indirect actions (e.g., through the carbohydrate-metabolism) would be impossible.

Light will intervene in the diurnal variation of the content (and total amount) of active principles, but again details of that intervention are not yet known. The effect of light is probably the greatest, as the other climatic factors, especially temperature, normally do not vary during a 24 hour period over such a range that they reach the minimal threshold, whilst for light, except in arctic regions, this does occur. Diurnal variations in the content are known for chlorophyll[26]. Hegnauer[27,28,29] has recently reviewed the investigations for several groups of active principles. For leaves of Solanaceæ with tropane alkaloids 5 authors found a greater content in the morning and 2 found a slightly greater amount in the evening and one no consistent variation. Since Hegnauer's paper, Hemberg and Flück[30] found for *Datura stramonium* a significant maximum in the leaves in the morning and in the roots in the evening, the contents being determined every 4 hours, calculated to the reference basis of crude fibre, fresh weight and dry weight. The reciprocity between leaf and root is in concordance with the fact that the tropane alkaloids are mainly produced in the roots. For digitalis, Hegnauer[28] found that of 8 authors, 4 found a maximum in the evening and a minimum in the morning, 2 did not find significant differences and one[31], a maximum at noon and a minimum at midnight. Due to difficulties and differences in the assay of digitalis, both chemical and biological, Hegnauer believes that the theory of a maximal activity in the evening has not been significantly refuted. With essential oils Hegnauer[31] stresses the special difficulties, due to factors like evaporation and resinification. Contradictory findings exist; Strepkov[32,33] found for *Salvia slarea* a minimal content in daytime and for *Trachyspermum ammi* (fruit) an irregular behaviour. Maxima in the afternoon had been found for *Salvia officinalis* by Tucakov[34] and recently by Schib[35] in a very careful investigation with 4 repetitions and 7 determinations during a 24 hours period. The latter results are calculated for dry weight, fresh weight and crude fibre. With regard to the evaporation in daytime which lowers both the percentage and the absolute content the conclusion that at least the final reactions on the formation of essential oil in *Salvia officinalis* take place in daytime becomes probable. Tschirikow[36] found minima in daytime for mentha; but he nevertheless believes that the formation of the oil takes place during the daytime. It may finally be mentioned that the photoperiodicity of the species (long day-plants and short day-plants) can also influence the diurnal variation. However, little attention has yet been given to that problem.

Considerable investigations have been performed with etiolated plants, especially on alkaloidal species. For young belladonna shoots[37] belonging to one clone, a 39 days' stay in darkness raised the alkaloidal content from 0·445 to 0·752 per cent. and the increase of protein nitrogen was even higher; considering that the dry weight must have fallen considerably one cannot conclude that the extra formation is due to the lack of light. With ricinus seedlings, etiolation produced a significant increase in the percentage of alkaloids[38,39]. That etiolation does not increase the percentage and especially the total alkaloids in all species has been proved employing lupinus seedlings, two investigations[40,41] demonstrating that with this species growth in the dark produces plants with significantly lower levels of alkaloids. Belladonna shoots devoid of chlorophyll increased the alkaloidal percentage considerably when illuminated[25].

Different strengths of sunlight (100, 68, 45 and 30 per cent.) produced significant increases of both total alkaloids and quinine in the roots of young plants of *Cinchona ledgeriana* (progenies of one single tree) at Puerto Rico. With maximum light, the yield was the highest and with 30 per cent. light, the lowest[42]. The alkaloids of the stem, however, were not affected significantly. The plants were grown on uniform soil, previously adjusted to 3 levels of nitrogen for each grade of sunlight. A much greater step in the increase of the alkaloidal content and the quinine content occurred between maximum light and 68 per cent. for the lowest amount of nitrogen, between 68 per cent. and 45 per cent. for the medium nitrogen content and between 45 and 30 per cent. for the highest nitrogen content which proves that the plants behaved differently in their reaction to light, if their nitrogen supply was different. With young (12–18 months) plants of *Cinchona succiruba*, de Moerloose[43] in using radioactive ^{14}C could show that light reduces the biosynthesis of alkaloids in the leaves; however, the bark showed no influence of light on the alkaloidal biosynthesis or storage[43].

For members of the Solanaceæ containing tropane alkaloids it has been known for a long time[44] that shaded plants produce drugs with a lower percentage of alkaloids and dry weight, than those grown in full sunlight. Stillings and Laurie[45] confirmed this and found also that the total alkaloids per plant were lower in shaded plants, a finding which the author[46] confirms, the difference found being about 25 per cent. for the percentage dry weight and 18 per cent. for the alkaloids per plant. *Scopolia carniolica*, another species among the Solanaceæ with tropane alkaloids, appears to react in a contrary manner to full sunlight because Schpilenjas' investigations revealed a higher content in plants grown in the shadow of trees than in those grown in maximum light[47]. Unfortunately the original publication was not available and in the abstracts no details are given. An explanation of the response of belladonna and scopolia may be that in their natural habitats belladonna prefers sunny conditions (e.g., clearings in the forests), while scopolia grows under the shadow of trees.

Contradictory reactions to light have been noted not only with related species but also for the same species. James[25] reports that in Connecticut, tobacco fields are shaded to produce thin leaves with a low alkaloidal percentage. On the other hand in young leaves on the tip of the plant the amount of nicotine per unit dry weight can be increased by shading[48]. The fact that the leaves shaded in Connecticut (and also elsewhere) are fully developed while the leaves in the second case are still growing may provide the reason for the opposite responses. Furthermore the reference base (dry weight) will probably also react differently.

The formation of the third type of solanaceous alkaloid, solanine, is intensified when potatoes are exposed to light. Fischer and Thiele[49] showed this increased intensity is produced over a wide range of wavelengths, while Conner[50] found it greater with short wavelengths (3000 Å) and smaller with visible light.

Several samples of the leaves of *Rhus copallina* and *R. glabra* contained an average of 2·8 per cent. less tannin, when grown in partial shade, compared with leaves grown in full sunshine[51].

A considerable number of investigations has been undertaken with plants containing essential oils. Several authors have combined the chemical assays for species of the Labiatæ with quantitative-microscopical determinations of the glandular hairs. Bode[52] made replicate determinations, every 7th day, of the essential oil content and of the ratio of glandular hairs to total epidermal cells of the leaves of sun-grown and of shaded plants of *Salvia officinalis*, during one period of vegetation. Except for the hottest weeks the difference in the oil content was very small, the sun-grown plants showing a slightly higher oil content. Yet in the hot period the oil content was up to 25 per cent. higher in the shaded plants when calculated with reference to the dry weight. With reference to fresh weight, the difference was of the same order, but much smaller. The glandular hairs were about twice as numerous for the sun grown plants. Bode[52] explains the lower oil content of the sun grown plants as being due to the higher rate of evaporation. Hegnauer[5] and his collaborator Bedaux[53] demonstrated that the glandular hair index was not only increased by a higher intensity of light, but also by a longer exposure to the light (9, 16 hours per day, continuous light). It seems that at least in a certain measure the total quantity of photo-energy has a determining influence on the glandular hair index. Schratz and Spanning[54] came to similar conclusions as far as the glandular hair index was concerned after using basil and 3 strains of peppermint, and Koelle[55] agreed for majoram. For the oil content, however, Schratz and Spanning found higher values. It is possible that the evaporation from salvia leaves is greater than that from peppermint and basil leaves. With basil, Lubimenko and Novikoff[56] found higher oil content which contradicts the results of Schratz. For ruta and laurus, however, the highest intensity of light produced the highest oil contents[56]. The writer regrets that he has not been able to read the original paper.

Rabak[57] in the United States and Sobolewskaja[58] in U.S.S.R. demonstrated for peppermint, that shading of the plants produced oils with smaller content of both free and esterified menthol, and a higher content of menthone. For a composite plant *Achillea millefolium*, Stahl[59] found a higher content of proazulene in sun-grown plants. Also in conifers the needles of sun-grown trees of tsuga species and of picea species from natural habitats yielded about 20 per cent. more oil[60]. Further indications about the influence of light on the essential oil content of plants are given in the works of Guenther[61] and of Gildemeister and Hoffmann[62], but very often without precise figures. Mostly it is stated that sunshine increases the oil content; but for some plants, as for *Elettaria cardamomum*, shade is important for a good growth and for a good oil content[61] (Vol. 5, p. 86).

Temperature

Few laboratory investigations are reported in which temperature alone was varied, and most of the results have been drawn from open-land cultures. Without doubt temperature is a major factor involved in research investigating the influence of various climates, especially of mountain climates and those of higher latitudes, for here temperature ranges are large and may become limiting.

Before dealing with the influence of temperature on drug plants a consideration of Lundegardh[3] (p. 144) may demonstrate how much the temperature may influence metabolic processes. Lundegardh states that for two groups of plants, which had been subjected to the same conditions for 24 hours and therefore produced equal amounts of photosynthetic products, i.e., carbohydrates, the rate of consumption of these by respiration and growth during the following night depended on the nocturnal temperatures. A difference of 10° C. over the 12 hours lowered the consumption of the plant at the lower temperature by 30 per cent. This means that on the following day metabolism had better starting conditions in plants which passed the night at lower temperatures than in plants which passed it at a higher temperature. This residual carbohydrate may have a favourable effect on secondary metabolic processes[16]. On the other hand processes that produce active principles during the night will produce these in a lower amount at the lower temperature.

In a greenhouse investigation, young plants of 2 species of cinchona were grown at temperatures 70–80° F., 65–75° F., and 60–70° F., the other conditions being the same[63]. For each unit the night temperature was lowered by 5° F. in order to produce more natural conditions. *C. pubescens* grew better at the highest temperature and showed significant variation of both total alkaloids and quinine in the stem and in the root, the increase in content being associated with the rise of temperature. *C. ledgeriana*, however, grew best at medium temperature but the alkaloids had no consistent relation to the alteration of temperature. Two closely related species therefore reacted in a different manner.

Aconitum napellus, *Atropa belladonna* and *Colchicum autumnale* among the alkaloidal plants and *Digitalis purpurea* and *D. ambigua* among glycosidal plants were assayed by Burmann[64], during 5 years in natural habitats. The annual variations of the results of all species were found to be proportional to the annual variations of the average annual temperatures. For *Zygadenus elegans*[65] a member of the Liliaceæ with alkaloids related to those of veratrum, the alkaloidal content of the leaves was found to be in direct proportion to the average daily temperature. Unfortunately details of this recent Russian investigation were not available to the author.

Anthocyanins[66] may be mentioned here. Even if they are not direct active principles of crude drugs, they are of some value for the estimation of several flower-drugs and they are related to active principles such as flavonols. With red cabbage, the rate of formation of anthocyanins increases considerably from 10° to 30° C.; however, at 30° C. the rate seems to be at an optimum, further rises of the temperature bringing about a decrease. This would correspond to findings of Beale *et al.*[67], that the anthocyanidines (with the exception of pelargonidine) are more abundant in temperate and alpine regions than in subtropical and tropical zones.

The importance of temperature for the rate of formation of essential oils is underlined by results from Paech's experiment[16] with *Asarum* *europaeum*. In plants grown at low temperature up to the moment where cell growth was completed, higher temperatures started a second period of formation of new excretion cells. Experimenting with plants containing fatty acids, Ivanow[68] and Schmalfuss[69] showed for linseed that in cold habitats the percentage of unsaturated fatty acids, especially linolenic acid, was higher, and Ruschkin[70] proved by laboratory trial that linseed when grown at night temperatures of 6 to 7° C. yielded oil, the iodine value of which was 6 to 7 units higher than from seeds grown at night temperatures of 13° C. In the same paper[68] is a finding that the seed oil of *Camelina sativa* and of *Helianthus* contains no linolenic acid when grown in warm climates, while it contains this acid when grown in cold climates[71]. The writer believes that in Russia an increase of the geographical latitude by 1° raises the iodine value 2 units. For *Pinus*, the same author[72] has pointed out, that the seeds of species growing in warm climates contain no linolenic acid and seeds of species with a cold habitat, *P. silvestris* and *P. cembra*, contain much of that acid. Also for olive oil, warmer growing-places yield oils with lower iodine value[73]. The problem of the influence of the temperature will be further discussed in relation with the discussion of various climates such as alpine or cold latitudes, etc.

Many indications based on field trials or even based on experiences drawn from agricultural production of drug plants attribute their special reactions to variations of temperature. These results must be interpreted with greatest caution, even if meteorological data are given in full. For *Artemisia absinthium* Rabak[74] in comparing drugs over a period of 10 years found great differences in the yield of oil from year to year. The meteorological data showed a close positive correlation between yield of oil and the average temperature, and in years with higher temperature the oil content was also higher. Mikhalow[75] found close proportionality between the oil content of peppermint and average temperature from year to year during the growth period yet the results refer to different states of development!

Water

Few results based on exact experiments on the influence of water have been published. Water occurs as rainfall, dew, humidity of the air and, as a secondary factor, humidity of the soil. All the 4 factors are more or less dependent on each other and they are also related to temperature. It should also be remembered that the plant has very effective means of regulating the intake of water from the soil as well as of the output by transpiration. Nevertheless, interactions of water on the production and on the content of active principles must be expected. As we have seen already in the section on the distribution of the chemical groups of active principles throughout the different climatic regions, active principles can have direct influences on the water content of the plant, e.g., essential oils on transpiration and mucilagenous substances on the retention of water.

No laboratory research dealing with the influence of humidity of the air on the content of active principles has come to the author's knowledge, only on soil moisture have some investigations been published. In these investigations sometimes the water content of the soil has been lowered so much that the plants began to wilt[77] which leads to a pathological reaction. Koelle[55] found a decrease in the number of glandular hairs per leaf, when the leaves had grown on a relatively dry soil; but as such leaves became smaller, the density of glandular hairs rose considerably, thus the leaf possessed more organs capable of producing essential oils for a given area. *Cinchona ledgeriana*[78] grew best on medium or high humidity soil, producing also significantly higher contents of total alkaloids and of quinine than on soil of low humidity.

Some investigations deal with the influence of heavy or light precipitations, without specifying the water content of the air and the soil. Based on a 3 years' investigation of 9 places in Germany, Boshart[17] concluded that abundant rainfall increased the content of essential oil in *Valeriana sp.* roots and *Coriandrum sp.* fruits and of both fatty oil and sinalbin in *Sinapis alba*. For *Mentha piperita* and for majoram abundant rainfall was disadvantageous for the yield of essential oils as was also insufficient rainfall, medium precipitations giving the highest percentage. However, it should be stated that the differences found were small and often not significant.

The literature contains many references to the influence of rainfall (mostly including humidity of air or soil). Usually, however, it is difficult to draw significant conclusions from these references, but the following may be quoted as examples.

Lemon grass (*Cymbopogon citratus*) when grown in the Belgian Congo[78] yielded about 0·2 per cent. of essential oil in the rainy season and about 0·35 per cent. in the dry season: the essential oil content of *Pimenta racemosa* grown in Puerto Rico varied between 1·32 to **2·02** to 3·40 per cent., the yield usually being inversely proportional to the rainfall[79]. Achmed and Fahmy[80] recorded significantly higher alkaloidal contents for *Hyoscyamus muticus* grown in the typical desert regions east and west of the Nile than for the same species grown in the more humid delta region.

Variations of the ratio of the individual constituents within the complex of active principles produced by variations of rainfall have also been recorded. Tornow and Fischer[81] compared the oils of peppermint, grown in 3 habitats each with 120 ml. of rainfall and one with only 20 ml. of rainfall. The content of free and esterified menthol was not significantly different. However, optical rotation of the latter oil was lower and specific gravity as well as refraction were higher, thus some special action of the dry climate on the composition of the oil must have occurred.

As might be expected, the amount of rainfall should differ during the different periods of growth of species, if drugs with high yields of active principles are to result. *Chenopodium ambrosioides* yields a high percentage of oil with a high ascaridole content only if rainfall had been abundant before flowering, but scarce during the ripening of the plant. Abundant rain during ripening produces a small percentage of oil with a low content of ascaridole[61] (Vol. 6, p. 154). In a careful investigation Rovesti[82] studied the oil content and several constituents of the oil, especially camphene, camphor and cineol and other factors of *Meriandra bengalensis* Benth., a

Labiatæ from Eritrea. The most interesting result is that the amount of oil (0·45 to 1·25 per cent.) and its content of camphene varied with the rainfall and vapour tension, whilst the content of camphor in the oil varied from 6 up to 70 per cent. inversely with the rainfall. Thus in months with low precipitations the amount of oil and the content of camphene were lowered, whilst the camphor content increased. In cultivated and irrigated plants as well as in plants grown naturally in the neighbourhood of water, the oil content and the percentage of camphene were high. These results are in some contradiction to the principles discussed for the distribution of the active principles in various climatic regions, as well as with the results from the density of glandular hairs in leaves. Rovesti considers this behaviour of meriandra as a typical reaction of the metabolism of essential oils to climatic factors.

He believes, furthermore, that the decrease of camphene and the increase of camphor at the beginning of the dry season is due to oxidation of camphene into camphor. It is, however, also possible that camphene evaporates and that camphor is freshly produced by the glands, and the author believes that this second possibility is the more probable one, especially with regard to the conditions in the gland itself. Nevertheless the relations between climate and composition of the active principles observed by Rovesti are of the greatest interest.

Another influence of humidity and especially of rain and dew is a destructive one for the active principles: Boshart[83] had noticed that leaves of datura when gathered in a wet condition yielded crude drugs with low assays. Gosh came to the same conclusion for ephedra[85]; Arens[85], Mothes[86], Engel[87], Sandfort[88] and Flosdorf and Palmer[89] proved that leaves can excrete both alkaloids and mineral salts through the epidermis and that these excreted substances may be washed off the leaves by rain or dew. This fact explains the low content in crude solanaceous drugs if they are harvested after or during rainy days.

Wind

The influence of wind has not been studied experimentally up to now in a detailed manner. For essential oils, the evaporation will be increased[90,91]. James[25] admits the possibility that in alkaloidal plants, such as tobacco, the increase of the transpiration may also increase the quantities of liquids brought up from the roots. And as alkaloids are mainly produced in the roots, it is possible—but not proven—that wind could increase in this way the content of active principles in the leaves of the plants concerned.

Influence of Special Types of Climate

Laymen, drug producers and even scientists often believe that special types of climate, e.g., the alpine one, would produce medicinal plants with the highest therapeutic value. Several researches and many inferences in the scientific literature may be found on these influences, yet significant results in this field are still scarce. This is due to the complications that are associated with the problem, such as the replaceability of ecological factors[6], the genetically differing strains within a species—especially with regard to their chemistry and to their reactions on external factors—the difficulty of controlling the diurnal, the seasonal and developmental variations during such investigations, the difficulties of interpretation, and factors like the high costs of such investigations.

Nevertheless the most important findings will be recorded here as far as the alpine climate (altitude), the climates of different geographic latitudes, oceanic and continental climates, are concerned.

For investigations of the influence of climate two main types of methods are possible[90,91]. The first is the assay of drug plants grown in natural habitats. As a result of the interactions and reactions to environmental factors, mentioned above, it will be realised that conclusions of general significance cannot be drawn from such an investigation unless a large number of results is available. Usually this is not the case and therefore those published are valid only for the particular conditions of the investigation. The second is the growth (and the subsequent assay) of medicinal plants strains, as genetically uniform as possible, on uniform soils or nutrient solutions, harvested at the same time and in the same state of development. Even with all these precautions, differences due to experimental conditions, may occur.

With both methods more than two places with different climatic conditions should be considered because only a curve based on more than 2 points can give an idea of the general trend followed by the variations in the content or composition of active principles.

Most of the published investigations deal with the influence of altitude and of these the larger proportion relate to the temperate zone.

The general variations, in climatic factors from the lowland to the mountains, are as follows.

Temperature: decrease of about 0·5° C. per 100 metres of altitude.

Radiation: increase of about 1 per cent. (g. cal./cm.^{2}/minute) per 100 metres of altitude. The increase is greater for ultra-violet, yet during the period of plant growth, the increase of ultra-violet is not much greater than that for other wavelengths; only in winter does this increase show a considerable difference.

Atmospheric pressure and density of the air: decrease.

Chemical composition of the air: practically unchanged up to 2000 metres, especially with regard to CO_2.

Cloudiness: dependent on local conditions.

Precipitations: increase, but this factor is very dependent on local conditions.

Relative humidity of air: decrease (50 per cent. per 2000 metres).

Wind: dependent on local conditions.

Of these climatic factors, only temperature may be reduced during the night in such a way that it descends below the minimum threshold for metabolic processes. All other factors will normally suffice for plant life at heights where drug plants grow naturally.

Great importance must be attached to the position of the slope. To give an example, at Zermatt barley is harvested on a slope at 2000 m.

facing South, while on the opposite slope only a conifer forest with lichens on the trees can exist.

For details of the behaviour of the general metabolic processes in the alpine climate see Lundegardh[3] and Schröter[93].

Only in a few of the investigations has the soil in the different climates been the same. Hecht[93–97] was the first to perform experiments on exchanged soils at Schatzalp near Davos (1800 m.) and Vienna (180 m.) in the years 1929 to 1932. Flück with his research students[90,98–102] undertook researches from 1933 to 1944 on 5 and later on 6 experimental stations in the valley of Arosa, Switzerland, at altitudes of 600 m., 940 m., 1250 m., 1460 m., 1840 m. and 2600 m. The climates of the 6 stations followed the general rules for climates with increasing altitudes, with one exception: at 940 m., due to orographic conditions, the temperature was about one degree higher than at the lowest station. Determination had been made first by the aid of thermometers and for the later years by the method of Pallmann[103], based on the splitting of sucrose.

Hecht had carried over soil from the alpine station to Vienna and vice-versa; however, only some of the experiments were performed on these exchanged soils and others on the natural soils of the two places. Flück *et al.* worked exclusively on the same soil on all stations. The soil was taken from the middle altitude and then carefully homogenised. From time to time all soils were renewed. The plants had been harvested as far as possible at the same state of development. Time of collection and method of desiccation have been the same for all harvests of a given series.

Rovesti[104,105] has on a smaller scale also transplanted species to different altitudes, the experiments being carried out on the natural soils.

Before dealing with active principles, it may be pointed out that chlorophyll is also present in different concentrations in different altitudes. Henrici[106] noted that for all plants she investigated, a lower percentage was found with increasing height and Zeller[107] found a decrease for *Gentiana rhætica* and *Aconitum napellus* but for *Pinus montana* and *Heliospermum alpestre* an increase in higher altitudes.

Of plants with alkaloids *Aconitum napellus* has been given greatest attention, probably because it is widely distributed in the Alps. Meyer[98] found on uniform soils, on the 5 stations mentioned above, a slight decrease in the old as well as in the young tubers and in the roots a decrease of 15 to 17 per cent. The mother plants for this experiment were gathered at about 2000 m. from a restricted area and they were uniform with regard to morphological characters. Hecht[97] also noted a slight decrease at his two different altitudes. More results deal with wild aconite. Brunner[108] and Flück[91], each on two slopes, found no consistent ratio between altitude and alkaloidal content. Métin[109] collected aconite roots in the Pyrenees 6 times during a period of vegetation at different altitudes and found in most of the series a definite increase at higher altitudes. On the other hand Dordi[110] and Marangoni[111] from Mascherpa's Institute at Pavia found in the Italian Alps between 350 and 2500 m. a constant decrease, while the toxicity was the lowest at 1000 m. Hegnauer[112] after a careful examination of all these results concludes that no general deduction concerning the ratio between alkaloidal content and altitude can be drawn for aconite at the present time and the writer agrees with him.

For plants with tropane alkaloids Handa *et al.*[113] reported for *Hyoscyamus niger* from several places in India, higher assay results for plants originating from altitudes above 5000 ft. and lower values for plants grown in the lowland.

For the opium poppy Annet[114] carried out a very careful investigation as early as in 1921. Pure strains grown around Cawnpore from the plains up to 2200 m. and during 4 successive seasons showed no consistent differences for the percentage of morphine or for the yield of latex per 1000 capsules. In higher habitats and in cooler seasons, however, more lancings were required to exhaust the capsules, thus demonstrating at least one influence due to climatic factors. On the other hand, Rovesti[105] found the following morphine contents in the capsules:

70 m.	.. ..	0·15 per cent. morphine.
350 m.	.. ..	0·188 ,, ,, ,,
600 m.	.. ..	0·195 ,, ,, ,,

The two investigations therefore arrive at contradictory results, which at the present time cannot be explained.

For cinchona it has often been believed that only in the mountains at relatively high altitudes did the alkaloidal content in the bark become high. As a matter of fact, in Java the cinchonas grow best from 1000 to 1600 m. (*Cinchona ledgeriana*, *C. succirubra* and *C. calysaya*) and from 1600 m. up to 2000 m. (*C. officinalis*)[115]. Moens[115] in the years around 1880 had already found no consistant influence within these limits and these results have since been confirmed by other authors[116,117].

In seeds of *Colchicum autumnale*, Venturi[118] noted a decrease up to 1600 m. while the bulbs showed no significant influence. For ephedra no relation could be found between altitude and alkaloidal assay[84].

Among plants with polymer carbohydrates only *Althæa officinalis* has been examined on uniform soils at high altitudes[100]. On vegetative propagants of 3 great plants, which had grown for 5 years at the highest station (1860 m.), the roots showed in 3 harvests typical optimum curves, the optima having occurred between 940 and 1440 m. For this species the reducing sugars were determined because they may be possible precursors for the plant mucilage. The sugar content was the highest at 940 m., which corresponded with the high content of mucilage. In the leaves the variations were considerably smaller and cannot be considered to be significant.

Ascorbic acid in the leaves of *Primula veris* and grown on the 6 stations previously mentioned varied over two years between 450 and 750 mg./per cent., the curve showing two minima, one at the hottest station (940 m.) and the other at the highest station. In wild grown leaves of the same species again a depression of the content occurred at 940 m.[102] At lower altitudes (500 m. to 900 m.) *Hippophaë rhamnoides* and rosa contained the greatest percentage at the highest and the smallest percentage in the lowest station[119]. The writer is of the opinion that from the rather narrow range of altitude no general conclusions should be drawn from these results.

For cardiac glycosides only a few results have been published. Marangoni[119] noted an increase in the potency at 6 habitats from 600 up to 1750 m. with *Digitalis lutea* and *D. ambigua*, while Hecht[97] records no significant difference of the potency for the two species mentioned and a decrease for *D. lanata* at the higher station.

Among plants with anthraquinone glycosides the small number of results do not allow any conclusion to be drawn[119].

The arbutin content of bearberry leaves from 10 natural habitats between 1000 and 2100 m. showed no regular relationship to the altitude at which the plant had been gathered[91]. After cultivation on uniform soils from 600 to 2400 m. over 4 years, the content of arbutin in the leaves of *Bergenia delawayi* varied similarly, but for the 5 lower altitudes large and small contents alternated from station to station. The greatest content was found at the highest altitude (2400 m.). The related species *B. crassifolia* behaved differently in that the arbutin content was greatest at altitudes between 1250 and 1860 m.

The bitter glycosides of gentian root increased regularly from 600 m. up to 1800 m.[99], while the bitter principles of *Artemisia glacialis* and *A. laxa*, decreased regularly in the leaves as well as in the flower heads[100]. The opposite behaviour of the two groups of bitter principles may be explained by the different chemical structure of the two groups. These reactions to the climate have been found to be the most consistent ones recorded up to now from high altitudes with plants grown on uniform soils, but further experiments should be carried out to investigate how far the reactions are similar in other regions of the Alps or other mountainous regions.

Anthocyanins were found to behave differently in 4 species, cultivated at the same places. When transplanted from 2000 m. in the Bernese Oberland to Zürich (450 m.), a 4 years' experiment showed in *Melandrium dioicum* and in *Campanula scheuchzeri* no significant difference at the two altitudes. *Epilobium angustifolium* contained significantly more anthocyanins at the higher station and *Viola calcarata* significantly less. Here again, for a closely related group of chemical substances two species were not affected by the two climates while in one species the content was higher and in another, lower at the alpine station and higher at the lowland station[120].

Tannins had been investigated in the Bergenias by Eymann[101]. In a research, extending over 4 years, two maxima were detected in *B. delawayi* (one at 660 m. and another between 1440 and 1840 m.), with a decrease at the intermediate stations as well as at the top station (2400 m.).

In a certain measure tannin behaved contrary to arbutin in the same plants, hence a low tannin content corresponded with a high arbutin content. In *Bergenia crassifolia* the content of tannin varied considerably from year to year.

Species with essential oils also produced different types of reaction at 5 to 6 stations (from 660 m. up to 2400 m.) when cultivated on uniform soils. In peppermint leaves (4 years[98,99]), in roots, rhizomes and stolons of *Peucedanum ostruthium* (4 years[101]) and in seedlings of *Thymus vulgaris* (1 year[98]), significant maxima of essential oil always appeared at the 940 m. station for which the highest temperature had been recorded. In thymus and peppermint the content decreased significantly on the lower and the higher stations up to 1840 m. Peucedanum, on the other hand, did not vary in its content of essential oil at the stations higher than 1250 m. in a significant manner. The oil content in the leaves and the flower heads of *Achillea millefolium*[99] at the same stations decreased in both organs but in the flower heads to a much greater extent. On the other hand the flower heads of *Achillea moschata*, which is a typical alpine species, growing naturally from 1000 up to 3000 m., the oil content was the highest between 1250 and 1440 m. with decreases in both upward and downward directions[100]. The curve was a typical optimum curve with one peak. In the fruits of *Carum carvi*, during two years, the greatest content was obtained at the lowest station and the smallest content at the highest station with a constant decrease except at 1240 m. where a second peak appeared[99]. Fruits from *Petroselinum sativum* ripened only up to 1250 m. and showed a significant decrease[99] in content while for the leaves the decrease was much less pronounced but could nevertheless be recognised[98].

From natural habitats *Thymus serpyllum* (flowering heads), *Carum carvi* (fruits from the same habitats for 2 years), *Juniperus sabina* (green parts of the twigs), *Artemisia laxa* and *A. genipi* never gave consistent ratios between content and altitudes[91]. For *Juniperus communis*, Ibanez[121] at 10 altitudes from 300 m. up to 1300 m. found a maximum at 700 m.

Angelica archangelica, when transplanted to 3 different altitudes near San Remo (20 m., 400 m., 800 m.), produced fruits and roots, which showed a marked increase in the oil content, the acid value and the ester value, while the optical rotation and the solubility in 90 per cent. ethanol decreased; the experiments were performed for one period of vegetation.

Many other contributions on species containing essential oils are recorded in the manuals of Gildemeister and Hoffmann[62] and of Guenther[61]; these mostly demonstrate that the yield from the plants is best at altitudes at which the plants grow well. These indications cannot, however, give any consistent argument for a clear effect of altitude on the oil content.

The variations in the content of active principles with climates of different geographical latitudes is also of interest. The climates at different latitudes may belong to different types and are not necessarily related to the latitude. Climatic conditions may be caused by other factors such as orographic conditions, general trends of the winds, distance from the ocean, etc. Only in great plains does the successive variation of climate, in the direction from the equator to the poles, show more or less regular alternations especially for the average temperature and also for radiation.

Many assertions on the influence of the climates of different latitudes (mostly designated as "northern" or "southern") have been made with regard to the content of active principles, but very few are associated with decisive measurements. If such influences exist, they have been caused predominantly by genetic reactions to the various conditions of the latitudes concerned.

For drug plants with essential oils it is often believed that in higher latitudes, such as northern Russia or Scandinavia, the yield of oil would always be low. Karma[122] reports on comparative assays of 12 samples of chamomile, originating from Yugoslavia (41 to 46°) up to Finland (65°). The highest assays were found with the Finnish and the Scandinavian drugs. Yet from these results it cannot be concluded that chamomile would always produce the highest contents in high latitudes, because from the many hundred assays for this drug, grown in more southerly countries, oil contents as high as 1·5 per cent. and even more have been noted. The results of Karma can only prove that even in high latitudes chamomile and probably also other aromatic plants are still able to produce high contents of essential oil. In a comparison of 9 plants of helichrysum collected between Sicily and northern Italy Rovesti[123] could not find a constant ratio between oil content and the latitude of the collecting places.

With regard to fatty oils, Ivanow[68] reports many investigations on linseed, grown over a wide range from North to South of the Russian plains. The yield of total oil was not so much affected, but the iodine value increased consistently with the increase of the geographical latitude. Detailed chemical investigations proved that this was mainly due to increasing percentages of linolenic acid in the oil. Ruschkin's[70] laboratory results, and many other investigations, show that decrease of temperature is responsible for the greater amount of unsaturated acids in fatty oils, grown in higher geographical latitudes.

Many other records on variations of active principles in medicinal plants with increasing geographical latitude can still be found. However, exact and reliable figures are scarce and it is considered necessary to wait before further discussion of the problem.

The most obvious difference between oceanic and continental climates is the much wider range between the maximal and minimal temperature of the latter compared with the former. Furthermore summers are dry in continental climates and humid in oceanic ones. Only a very few publications deal with the reaction of the active principles of medicinal plants to these types of climate. From a recent experiment[124] 7 strains of *Duboisia myoporoides* with the alkaloidal complex having a different chemical composition and originating from regions with different climates (temperate to tropical) were transplanted to the continental climate of Canberra and to the oceanic climate of Nambour (Queensland). The yield of alkaloids as well as the composition (several strains very rich in hyoscine, and the others very rich in hyoscyamine) was not significantly affected by the different climates. The experiment has been continued for 3 summers in Canberra and for one winter and one summer only in Nambour. Nevertheless it can be said that no significant influence of the two climates can be seen in the results.

"Climatic Strains" and Active Principles

Much argument has arisen on the question of whether different climatic strains exist from a Linnean species. In such discussions, it should be always taken into account that in natural habitats the climatic factors alone will not decide on the chemical composition of the plants, but that all environmental factors act in a combined manner. It may be that in some cases the climatic factors are the most decisive ones. But it must be stressed that it would be more correct to speak of strains of the habitat or perhaps of geographical strains.

Some examples of strains within one species differing mainly in their chemical composition may be mentioned. For *Duboisia myoporoides* the two strains, designated as "northern" (rich in hyoscine) and "southern" (rich in hyoscyamine) have been distinguished[125,126]. The authors stress however, that in their opinion, although environmental factors may be of some importance, the genetic factors are the more important ones. Webb[8] has shown how the genetic factors may have influenced the selection during the establishment of the strains in the regions they occupy to-day.

Within the area of natural habitats of *Strophanthus sarmentosus*, Reichstein *et al.*[127,128] found in western tropical Africa 4 chemically different types, containing mainly sarmentogenin, sarmutogenin, sarverogenin and a fourth type which contains only a very small quantity of glycosides. The four types grow predominantly in different geographical regions, and the question was whether the climatic factors were responsible for the chemical differences within the 4 strains. Yet the geographical distribution of the strains is not strictly confined to the regions in which they occur predominantly, intermediate types with regard to the chemical composition being also found. It has been reported that in some cases individuals of one type may be found in the region of another type. This is, of course, a strong argument against the opinion that the species *S. sarmentosus* would react immediately to different habitats by variations of the composition of the glycosidal complex. It is the writer's opinion further that the actual distribution of the chemical types is the result of a natural selection. It is not very probable that the aglycones or glycosides can have had a decisive influence during this selection, yet nothing is known with certainty on this problem. Other properties of individuals of the original population of the species *Strophanthus sarmentosus* (which is a very polymorphic species with regard to the morphological characters) may have had a greater influence during the selection along the many thousands of years. It may be that these other properties are genetically linked with the genes that control the formation of the different glycosides, and by this means the different strain may have developed.

In careful and valuable investigations Rovesti[129,130] demonstrated that in Eritrea *Meriandra abyssinica* Benth. comprises two strains that are chemically different, one rich in menthone and another rich in citral. For *Ocimum menthæfolium*, 4 strains are distinguished (one rich in camphor, one rich in citral, one rich in menthone and one rich in pulegone). The opinion has been expressed that these types, which may also differ slightly in morphological characters, could be the products of direct reactions to environmental factors and Rovesti speaks of "Varietas physiologica" but also of "Ecotype". But the habitats of the various types are different also in climatic factors (humidity, temperature, etc.). Unless the behaviour of the types has been investigated by transplantation into the other environmental conditions and unless the genetical behaviour of the types has not been examined, it is considered that the types found by Rovesti are at least partly the product of a long selection and not wholly an immediate and direct response to the environmental factors.

The fact that in various regions the composition of the active principles of one species varies, at least quantitatively, has also found practical application. The most recent applications in this field are the efforts of the Department of Social Affairs of UNO to determine the origin of opium with the aid of quantitative differences in the proportions of the alkaloids, especially the minor alkaloids such as porphyroxin; here again, not only climatic factors control this composition.

With regard to the existence of strains which are chemically different within a Linnean species, chemists should be aware that for a long time the taxonomists have divided the species into groups that are morphologically different. If taxonomists have not taken into consideration the differences in the chemical composition, this may be at least partly due to the vast amount of experimental work necessary to make such differentiations. But this problem is outside the scope of the subject discussed here.

In concluding, the writer wishes to stress once more that the response of plants to the environmental factors is an extremely complex one. Certainly the climate has its influences on the formation and content of active principles. However, the present state of our knowledge does not allow general rules or conclusions to be drawn, except one: the plants produce their maximal content of active principles under those climatic conditions which allow the optimum development of the plant itself. Special combinations of climatic and other environmental factors may always produce exceptional contents of active principles. However, the most important factors that affect the content and the composition of the active principles in medicinal plants are not climatic ones, but the genetic ones.

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