生薬基原植物鑑別情報のデータベース化

日本薬局方の生薬総則の項に「生薬の基原は適否の判断基準とする」と明記されているとおり，生薬の品質管理において，基原植物の正しい鑑別はその根幹をなすものである。総合DB構築プロジェクトの遺伝子鑑別情報パートでは，基原植物の鑑別，優良品種の選抜などに応用可能な遺伝子情報を集積し，データベースとして管理・提供することを目的とし，富山大学，国立医薬品食品衛生研究所生薬部をはじめとする生薬の遺伝子解析のエキスパートの先生方と共同で，遺伝子鑑別情報のデータベース化に取り組んでいる。

遺伝子情報の品質管理への寄与は今後いっそう高まると考えられるが，総合DBでは，重要生薬及びその基原植物について，鑑別に適した遺伝子領域の検討及び市場流通生薬の遺伝子鑑別データの収集を進めており，各種データの集積により，市場の生薬の流通実態に即した基原植物種の遺伝子鑑別法が整備され，生薬の品質の確保に貢献できるものと考えている。

「バーコード化」と生薬遺伝子鑑別

現在，地球上のあらゆる生物の同定のため，特定の遺伝子領域の塩基配列情報を集積する「バーコード化」プロジェクトが進められている。本プロジェクトは国際コンソーシアム Consortium for the Barcode of Life (CBOL) により進行中であり，その中の植物ワーキンググループにより，陸上植物については遺伝子マーカー2領域（*rbcL, matK*）の組み合わせによる植物種同定が提唱されている。薬用植物の基原植物鑑別も一種のバーコード化であるが，すでに中国では薬用を含む植物を対象としたバーコード化を猛烈なスピードで進めている。生薬については，国産及び国内に流通する生薬が遺伝子鑑別情報的に「傍流」となることのないように，総合DBで収集中の生薬の鑑別に関する遺伝子情報についても国際塩基配列データベース DDBJ/EMBL/GenBank への登録等による発信を行うとともに，国際的な情勢を注視していく必要があると考えている。

ポストモデル植物時代の薬用植物のゲノミクス

植物より得られる有用物質の多くは二次代謝産物であるが，それらは各代謝経路にほぼ特異的な生合成酵素群によって生合成される。その遺伝子レベルの設計図となるのがゲノムDNA情報であるが，二次代謝産物に富む薬用植物のゲノム情報は，ほとんどが未開拓のまま残されている。シロイヌナズナ，イネといったモデル植物のゲノム解読が完了したポストモデル植物時代の今日，研究者は非モデル植物の遺伝子解析，そして比較ゲノム解析に向かっているが，Genomes Online Database (GOLD) によると，生薬として利用されるような薬用植物についてはゲノム解読の完了した植物はイネを除き未だ現れていない。しかしながら，ブドウのようにゲノム解読が完了した植物は着実に増えており，薬用植物では，ウラルカンゾウ，オタネニンジン，サンシチニンジンのゲノム解読が中国で進行中である。

表　主な薬用植物のEST登録数

ウラルカンゾウ	50,666
ショウガ	38,115
イチョウ	21,590
ケシ	20,815
ニチニチソウ	19,910
ウコン	12,593
オタネニンジン	11,412
セリバオウレン	903

NCBI dbESTより 2011.10.1現在

また，ゲノム情報に加えて有用な遺伝子情報と考えられるのが，生合成遺伝子をはじめとする生体試料における全発現遺伝子の情報を集積した Expressed Sequence Tag (EST) 情報である。こちらは，近年，薬用植物においても多種のライブラリーが構築されており，米国NCBIのdbESTによると表のような植物種についてデータが集積されている。

次世代シーケンサーの登場により，大規模遺伝子解析は容易になりつつあり，今後，研究者がゲノム解析から軸足を薬用植物等非モデル植物のEST解析や比較ゲノム解析に移し，解析される植物種と蓄積される情報は量と質の両面において大幅に充実していくものと予想される。当センターにおいては，平成22年度より薬用植物のESTライブラリー構築を開始し，初年度はケシについてライブラリー構築を行い，現在，データ公開に向け推定酵素機能のアノテーション等を精査しているところであるが，今後，国内においても，薬用植物を対象としたEST解析そして比較ゲノムプロジェクトが誕生することが切望される。薬用植物の網羅的な遺伝子情報の整備により，生合成研究のみならず，優良系統のマーカー探索等々の研究に新たな道筋が示されると期待される。

おわりに

遺伝子情報を中心とした関連情報を網羅的に扱うゲノミクスは，医療分野ではオーダメイド医療の基盤となるファーマコゲノミクス，そして食品分野では栄養学と遺伝子や代謝物情報等の融合であるニュートリゲノミクスへと展開している。生薬・漢方薬の分野においても，遺伝子情報をベースに基原・産地・成分情報などを網羅的に集積した，言わば「生薬ゲノミクス」は，生薬および薬用植物の品質確保，有効利用の未来を築く礎のひとつとなるものと考えられる。センターで構築中の生薬の各種関連情報を統合した総合DBは，まさに生薬ゲノミクスの中核をなすデータベースとして真価を発揮できるものと確信している。当センターの保有する優れた薬用植物資源を，総合DBの多様な情報と共に活用していただければ幸いである。

なお，次号では当センター筑波研究部栽培研究室の渕野裕之室長から寄稿していただく予定です。

〈寄　稿〉

漢方薬に使用される生薬・薬用植物の現状

独立行政法人 医薬基盤研究所 薬用植物資源研究センター長　川原 信夫

1．はじめに

平成22年10月、生物多様性条約第10回締約国会議（ＣＯＰ10）が名古屋で開催され、生物資源を巡る利益配分に関する議論が大きな話題を呼び、薬用植物の国内栽培化の推進ならびに生薬の安定供給の重要性が再認識されています。一方、生薬類の品質、規格に関しては平成18年に第15改正日本薬局方（以下、JP15）が施行され、生薬関連分野では６種の漢方処方エキスが新規収載される等、大きな改正が行われました。日本薬局方生薬等委員会では引き続きJP15第一追補（平成19年10月施行）および第二追補（平成21年10月施行）を通じて新規収載品目の選定、各種試験法の検討、規格値の設定等について検討を行い、平成23年４月には第16改正日本薬局方（以下、JP16）が施行されました。

本報では、最初に漢方エキス製剤の製造工程ならびにそれら製剤に使用される生薬類について概説します。続いて漢方処方を構成する生薬類について、日本漢方生薬製剤協会（以下、日漢協）が行った最新の調査結果に基づく生薬・薬用植物の生産・流通および価格変動の現状ならびにJP16に収載される生薬類の品質、規格に関する最近の動向について解説します。さらに、生薬・薬用植物の国際調和について概説した後、筆者が所属する独立行政法人 医薬基盤研究所 薬用植物資源研究センター（以下、センター）の薬用植物資源に関する近年の取り組みについて紹介します。

2．漢方製剤に使用される生薬の種類

生薬とは、動植物の部分・細胞内容物・分泌物・抽出物あるいは鉱物で、そのまま薬品として用い、あるいは製薬の原料とするものです。平成20年度に日漢協所属会社が漢方製剤等に使用した生薬は248種で、これらのうち219種が植物由来、19種が動物由来、鉱物および菌類由来が各５種であり植物由来の生薬が中心となっております。また、医療用漢方製剤148処方では120種の生薬が使用されています。

3．漢方エキス製剤の製造工程

漢方エキス製剤の製造工程は、まず原料生薬を破砕、切断後、各種処方に応じて生薬を調合し、抽出を行います。さらに固液分離、濃縮、乾燥の工程を経て、エキス原末を製造し、最後に賦形剤等を加えて製剤化を行い、アルミパックなどに包装して漢方エキス製剤が完成します。一方、原料生薬を破砕、切断後、調合し、煎じ器等で抽出を行う煎じ薬もあります（図１）。

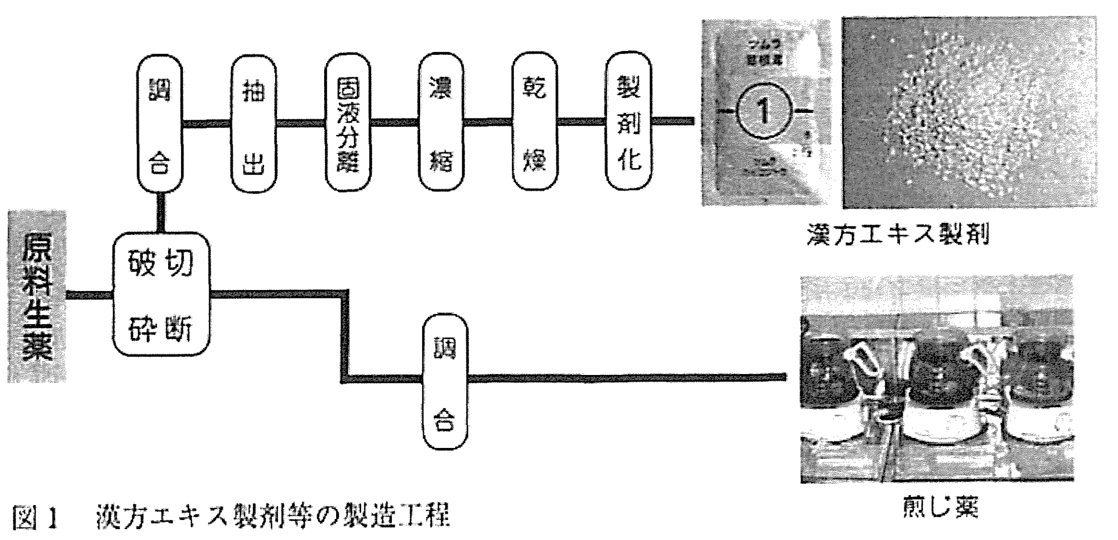

図１　漢方エキス製剤等の製造工程

4．生薬の生産、流通の現状

漢方製剤等の生産金額は、平成19年現在、約1230億円であり、医薬品総生産金額に占める割合はおよそ２％程度です。また、漢方製剤等の生産金額のうち75％は医療用漢方製剤です（図２）。さらに近年、漢方製剤等の生産金額は微増傾向にあり、これは新型インフルエンザや認知症等に漢方製剤が使用されはじめていることが理由の一つと考えられます。一方、生薬・薬用植物の用途は、医薬品類をはじめ化粧品、香料、食品等、多岐にわたっており、これらの原料として使用される生薬の多くは海外からの輸入に依存していることは周知の事実です。これらを示す具体的なデータとして財務省貿易統計、財団法人特殊農産物協会作成の資料等があり、その大枠を推察することが可能ですが、漢方生薬製剤として使用される原料生薬の数量は比較的最近まで把握できていない状況でした。近年、日漢協では原料生薬の流通データの重要性を鑑み、回答が得られた調査対象会社74社に対し生薬276品目について平成20年度における医薬品原料として使用した品目ごとの数量および入手相手国の調査を行いました（８頁表参照）。この結果、全体の使用数量は約２万トンで、海外から入手している数量は約1.8万トン、その内中国からは約1.7万トン、日本は約0.2万トンであることが判明しました。パーセンテージに換算すると中国83％、日本12％、その他の国５％であり、これはすなわち日本における生薬の自給率が12％であることを示しています。調査対象276品目のうち使用実績のあったものは248品目で、日本のみは22品目、日本および中国43品目、日本およびその他５品目、中国のみ113品目、中国およびその他28品目、日本および中国・その他19品目、その他のみ17品目との結果を得た。中国から入手している生薬は数量ベースで83％、品目数ベースで203／248品目に及んでおり中国への依存度が高いことが改めて示されました。これに対し、日本での入手は数量ベース12％ですが、品目数ベースでは89／248品目となっており種類では約４割近くの生薬が国内で生産されていることが明らかとなりました。

また、数量における頻度として、上位52品目が全体の90％を占めており、上位117位でその頻度は99％に達しており、品目の半数以上が数量の１％に集中していることも判明しました。使用実績のあった248品目のうち、148品目がJP収載生薬、37品目が日本薬局方外生薬規格（以下、局外生規）収載生薬でした。これを数量ベースで換算するとJP収載生薬は92％を占め、局外生規収載生薬を合計すると94％に達しました。従って、我が国では医薬用原料として数量ベース94％の生薬がJP等の公的基準の中で管理されていることが確認されました。

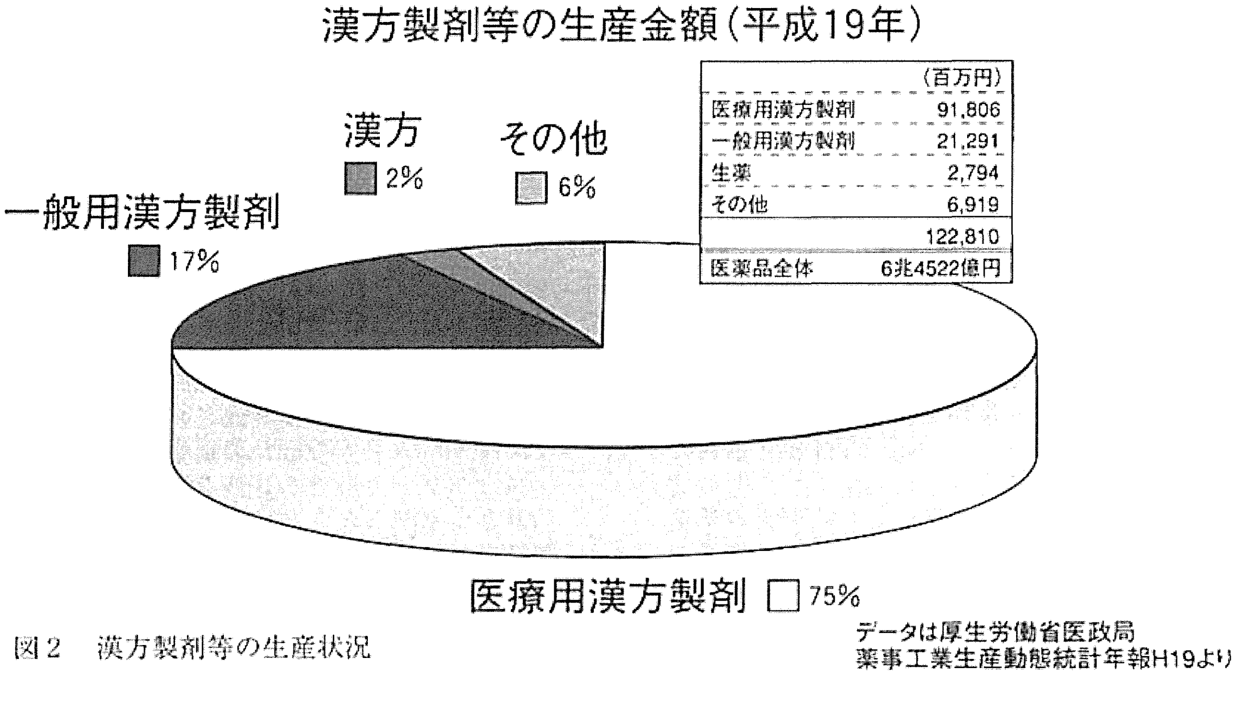

図２　漢方製剤等の生産状況

5．生薬の品質、規格の動向

JP15が施行されて以来、現在までにJP15第一追補（以下、JP15-I）、JP15第二追補（以下、JP15-II）およびJP16において生薬の品質、規格に関する改正が順次行われております。以下に生薬および漢方処方エキスに関する主な改正点を示します。1）**新規収載品目**：サンザシ、ゼンコ、ドクカツ、ビャクゴウ、ヤクモソウ、ウコン末、エンゴサク末、桂枝茯苓丸エキス、半夏厚朴湯エキス（JP15-I）、カッコウ、ニクズク、ボクソク、リュウガンニク、ローヤルゼリー、リュウコツ末、牛車腎気丸エキス、真武湯エキス、八味地黄丸エキス（JP15-II）、カッセキ、コウイ、コウベイ、ゴマ、黄連解毒湯エキス、柴胡桂枝湯エキス、柴朴湯エキス、芍薬甘草湯エキス、十全大補湯エキス、小柴胡湯エキス、小青竜湯エキス、無コウイ大建中湯エキス、釣藤散エキス、麦門冬湯エキス、六君子湯エキス（JP16）、2）**英名、ラテン名、基原・本質の表記整備**：リュウコツ（JP15-II）、インヨウカク、キョウニン、コウカ、コウボク、シンイ、ソウジュツ、チンピ、ボウイ、ウワウルシ、カンテン、ゴシュユ、サンソウニン、シゴカ、ショウマ、ハチミツ、ハマボウフウ、ビャクシ、ビャクジュツ、ブクリョウ、ボウフウ、ウイキョウ油、コンズランゴ（JP16）、3）**生薬の性状の表現改正**：ジオウ（JP15-I）、アマチャ、カッコン、キササゲ、タクシャ、タクシャ末、チョレイ末、トチュウ、ボレイ、ボレイ末（JP16）、4）**新規確認試験法の設定**：エンゴサク（JP15-I）、オウギ、ボウフウ、ソヨウ（JP15-II）、5）**確認試験法の記載変更、追加**：キョウニン、トウニン、トウニン末、オウゴン末（JP15-I）、ウコン、サイコ（JP15-II）、ビャクシ、オンジ、オンジ末、コウジン、ニンジン、ニンジン末、トウニン末（JP16）、6）**新規成分含量測定法および定量法の設定**：キョウニン、トウニン、トウニン末、ウコン、ウコン末、ソヨウ、サンシュユ（JP15-II）、チンピ（JP16）、7）**新規純度試験法の設定**：ユウタン（JP15-II）、8）**純度試験における重金属限度値の設定**：46品目（JP15-I）、11品目（JP15-II）、9）**純度試験におけるヒ素限度値の設定**：59品目（JP15-I）、2品目（JP15-II）、10）**薄相クロマトグラフィー用生薬の新規収載**：シャゼンシ、ゴシツ（JP15-II）、11）**参考情報の新規収載**：遺伝子情報を利用する生薬の純度試験（JP15-I）、日本薬局方収載生薬の学名表記について（JP16）。さらにJP16において成分含量測定法は、サフランを成分含量に変更することを除きすべて定量法に置き換えられました（35品目）。

なお、各種日本薬局方情報は医薬品医療機器総合機構のホームページ（http://www.pmda.go.jp/kyokuhou.html）に掲載されており、pdfファイルのダウンロードが可能です。

6．生薬・薬用植物に関する国際調和への取り組みについて

各国で使用されている生薬に関する情報を収集、整理し、共通認識を得ることは生薬・薬用植物の国際調和の観点から非常に重要です。このような背景のもと、西太平洋地区の6カ国7地域（日本、中国、韓国、ベトナム、シンガポール、オーストラリア、香港）の生薬・薬用植物の安全性、有効性および品質に関する技術的な記録とコンセンサスを提供することを目的として「生薬・薬用植物に関する国際調和のための西太平洋地区討論会」（FHH：Western Pacific Regional Forum for the Harmonization of Herbal Medicines）が設立されました。著者らは、日本、中国、韓国およびベトナム4カ国の薬局方に収載された共通生薬の試験法および規格値に関する比較表の作成および確認試験法に収載されたTLC条件ならびに定量法（成分含量測定法）に収載された分析条件ならびに生薬関連一般試験法の詳細についての比較検討を行い、得られた各種情報に関する比較表を作成し、それらをとりまとめた冊子体を刊行しました。さらにこれら比較表のpdfファイルをFHHホームページ（http://www.fhhm.net）ならびに国立医薬品食品衛生研究所ホームページ（http://www.nihs.go.jp/dpp/FHH/FHH.htm）にアップし、公開を行っています。今後は各国薬局方の改正に伴い、順次比較表の更新を行う予定です。

7．独立行政法人 医薬基盤研究所 薬用植物資源研究センターにおける薬用植物資源への取り組みについて

センターは、平成17年4月に国立医薬品食品衛生研究所薬用植物栽培試験場から組織変更され、独立行政法人医薬基盤研究所の生物資源部門として新しいスタートを切りました。

センターは、北海道研究部（名寄市）、筑波研究部（つくば市）、筑波研究部和歌山圃場（日高川町）および種子島研究部（中種子町）の3研究部1圃場から構成されています。当センターは、日本で唯一の薬用植物リファレンスセンターとしての機能を果たすことを目的とし、研究者ならびに行政に提供する薬用植物等に関する情報整備、研究・開発資源としての薬用植物等の収集・維持・保存を行っています。さらに有用性の高い新品種の育成ならびに薬用植物栽培の機械化による栽培の低

コスト化の実現および薬用植物等に含まれる生理活性物質の探索ならびに薬用植物有効成分の生合成に関与する遺伝子の解明とその遺伝子操作等による成分の改変等への応用を行っています。

以下にセンターの薬用植物資源業務ならびに研究について簡単に紹介させていただきます。

1）薬用植物資源の収集、保存、情報整備および行政的要請への対応

①薬用植物資源の収集・維持管理

センターでは約4,000系統の植物を栽培・維持すると共に、種子交換・保存用種子の採取、収集を行い、現在約13,000点の種子を各種温度において保存し、適宜発芽試験等も実施しております。

②ソロモン諸島有用植物調査

平成20年度より高知県立牧野植物園が中心となって開始された文部科学研究事業の分担研究機関として、ソロモン諸島の植物調査を行い、現在までにさく葉標本7,084点、化学分析用サンプル507点、生植物標本230点および種子標本53点を収集し、維持・管理しております。

③薬用植物資源の提供および行政支援対応

種子交換目録（Index Seminum 2005-2011）を年度毎に作成し、平成22年度は397機関（62カ国）に送付し、その請求に対し1,147点（81機関）の種子を送付しました。また、種子交換以外での薬用植物資源提供実績として、大学および公的研究機関等に対して、平成18～22年度の５年間に種子480点、植物体497点、標本139点および分析用サンプル1,398点を供給しております。

④薬用植物栽培・品質評価指針の作成

イカリソウ、エンゴサク、カキドウシ、クソニンジンおよびトウガンの５品目について「薬用植物　栽培と品質評価」Part12の原稿を作成し、刊行しました。

⑤薬用植物データベースの構築

センター保有の重要薬用植物等100種について、各種情報をデータベース化し、平成22年3月31日より公開しております。
(http://wwwts9.nibio.go.jp/mpdb.html)

2）薬用植物等の保存、増殖、栽培、育種に必要な技術ならびに化学的、生物学的評価に関する研究開発

①薬用植物資源の新品種育成に関する研究

有用性の高い新品種の育成を目的として薬用植物の育種に取り組みハトムギ新品種「北のはと」、「はとろまん」およびシャクヤク新品種「べにしずか」の育成に成功しました。

②薬用植物資源の系統選抜および大規模機械化栽培による薬用植物の低コスト栽培法の確立に関する研究

薬用植物等の種々の増殖法に関する検討及び野生あるいは国外産薬用植物の国内栽培化を目的として、カンゾウの高グリチルリチン酸含有系統の育成を行い、日本薬局方規格値を超える系統９種の選抜に成功しました。さらに大規模機械化栽培による薬用植物等の低コスト栽培法の確立に関しては、野菜類の収穫、選別および洗浄等に用いる既存の農業機器を薬用植物等の栽培および調製に応用し、一部の機器において充分適用可能であることが確認されています。

③薬用植物資源培養物等の長期保存条件の検討に関する研究

植物組織培養物の超低温保存に関する研究では、継代維持中の薬用植物カルスを材料にガラス化法による超低温保存条件を検討し、数種の薬用植物において高頻度の再生に成功しました。

④薬用植物資源の養液栽培ならびに遺伝子導入技術に関する研究

カンゾウの養液栽培において、約400日間の栽培期間で日本薬局方規定値を満たす系統の作出に成功しました。またセリバオウレンおよびベラドンナの形質改変を行い、単位容積あたりのアルカロイドの生産効率の向上に成功しております。

⑤薬用植物資源の各種活性スクリーニングに関する研究

薬用植物エキスの抗リーシュマニアスクリーニングを継続的に行い、特にペルー産薬用植物からは数種の新規化合物を含む種々の活性化合物を単離、構造決定しております。

3）今後の展望

センターでは第２期中期目標を策定し、平成22年４月から新たな５カ年計画による研究業務が開始されています。今期は新たに薬用植物ファクトリーおよび薬用植物ESTライブラリーに関する応用研究を行う予定です。さらに平成22年度から厚生労働科学研究事業「漢方薬に使用される薬用植物の総合情報データベース構築のための基盤整備に関する研究」も採択され、薬用植物総合データベースの構築に関する研究がスタートしています。

8．おわりに

今回、日漢協のご厚意により生薬・薬用植物の生産・流通に関する重要かつ詳細なデータを示すことができました。また、生薬および漢方処方は保健衛生上重要かつ有用な医薬

品であり、その品質を確保し、常に良質な製品を供給していくためには、適正な規格設定が必須です。引き続き日本薬局方生薬等委員会では、第17改正日本薬局方の作成に向けた検討を行っております。さらに近年、生薬・薬用植物を巡る国際調和の動きも加速しています。その中で日本は、各種情報の集積、発信を通じて中心的な役割を担っております。

一方、センターでは、薬用植物の資源保護・系統保存、栽培・育種研究等、民間企業では実施できない研究事業を展開しています。特に現在までにセンターに導入された生きた資源植物は、遺伝資源としていわば何物にも代えがたい宝です。これら貴重な植物資源を大切に栽培、系統保存することがセンターに与えられた重要な責務であると強く認識し、今後も職員一丸となって一層の努力を注いでまいります。

謝辞

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表　医薬品原料として使用された生薬の使用量と供給国（平成20年度）

単位:kg

No.	生薬名	使用量	供給国 日本産	供給国 中国産	供給国 その他
1	カンゾウ	1,267,395		1,267,395	
2	シャクヤク	1,164,126	41,019	1,123,107	
3	ケイヒ	1,033,793		836,645	197,148
4	ブクリョウ	896,311		861,722	34,589
5	タイソウ	675,997		675,997	
6	ハンゲ	629,063		629,063	
7	ニンジン	610,092	498	608,946	648
8	トウキ	580,607	204,471	376,136	
9	マオウ	568,686		568,686	
10	コウイ※1	555,718	555,718		
11	カッコン	553,999	61	546,098	7,840
12	ソウジュツ	501,647		501,647	
13	ヨクイニン	449,253	600	373,528	75,125
14	サイコ	443,811	23,244	399,212	21,355
15	ダイオウ	439,590	95,418	344,172	
16	ビャクジュツ	427,357		419,624	7,733
17	センナ	426,230			426,230
18	ジオウ※2	397,512	2,715	394,659	138
19	オウゴン	383,969	15	383,954	
20	セッコウ	380,348		380,348	
21	センキュウ	373,432	313,739	59,693	
22	タクシャ	358,951		358,951	
23	ショウキョウ	343,660	162	343,408	90
24	カッセキ	297,806		297,806	
25	ボタンピ	285,726	37	285,689	
26	オウギ	283,727	12,555	271,172	
27	キキョウ	268,651		268,586	65
28	クマザサ葉	240,000	240,000		
29	チンピ	232,043	133,975	98,068	
30	カンキョウ	215,833		215,833	
	上位30品目合計	15,385,333	1,624,227	12,990,145	770,961
	総合計（248品目）	20,274,022	2,477,611	16,829,773	966,638
			12.2%	83.0%	4.8%

※1:コウイはマルトース含む　※2:ジオウは熟ジオウ含む

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"The forefront of research on natural medicines"

Innovative cultivation: Hydroponics of medicinal plants in the closed-type cultivation facilities

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1. Importance of hydroponics of medicinal plants in the closed-type cultivation facilities

Medicinal plants synthesize substances that are useful to human and animal health. Most of the substances are so-called secondary metabolites, such as alkaloids, terpenoids, phenols, *etc.* Medicinal plants have been the important source of modern allopathic medicines as well as the crude drugs for traditional herbal medicines such as Kampo (Japanese traditional herbal medicine). Approximately 20,000 tons of crude drugs are used annually as pharmaceutical ingredients in Japan. However, Japan's self-sufficiency rate for crude drug is only 12% according to the inspection performed by the Japan Kampo Manufacture Association (JKMA) in 2008.[1] Therefore its constant and stable supply is threatened; in fact, import of ephedra and licorice (glycyrrhiza) is restricted. In general, medicinal plants need long-term cultivation and require considerable human labor that such tendencies would lead to a decline in domestic cultivation further enhanced by the aging farm-workers. In addition, constitution and concentration of active medicinal ingredients in crude drugs are largely influenced by factors such as growth environment, genetic background, harvesting time, drying, storage and processing methods of medicinal plants.

Under these circumstances, sufficient and stable supply of medicinal plants which are well-identified and of high quality enable us to secure high value medicinal resources. This largely contributes to our present and future medical care. For this purpose, hydroponics of medicinal plants in the closed-type cultivation facilities that can optimally control the growth environment is one of the effective solutions. If this kind of cultivation becomes possible, it would prevent overharvesting of wild medicinal plants and improve the integrity of the native habitat. In this cultivation system, non-agrochemical and non-radiation contaminated plant materials could be produced and multilateral and less labor cultivation become possible by appropriate entrance and exit managements, and by systematic and sophisticated cultivation. Furthermore, it might promote domestic production of medicinal plants.

Glycyrrhiza, referring to the dried root and stolon of *Glycyrrhiza uralensis* (leguminous perennial plant, Chinese licorice), is the most frequently prescribed crude drug in Kampo medicines (over 70% of commercialized Kampo formulations contains Glycyrrhiza in Japan). Glycyrrhizin (glycyrrhizic acid) extracted from glycyrrhiza is generally used as curatives for liver and allergies, and as a natural sweetener. Circumstances referring to the supply of *G. uralensis* and the merits of hydroponics are summarized in Figure 1.

2. Hydroponics for medicinal plants whose underground parts are utilized

Although hydroponic studies on medicinal plants have been performed at a laboratory level, most of them were on the plants whose terrestrial parts (leaf, stem and

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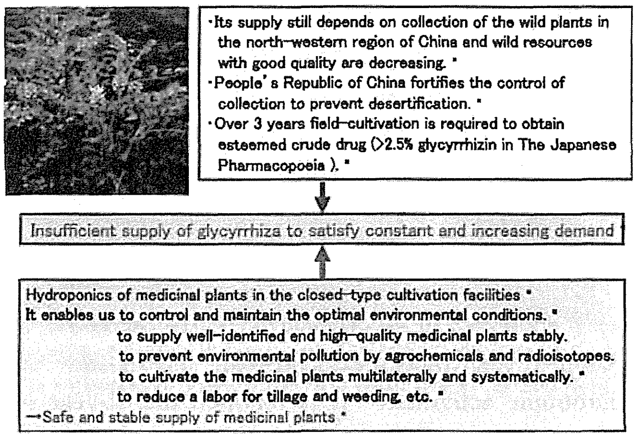

Figure 1 Circumstances around *Glycyrrhiza uralensis*

flower, *etc.*) are utilized. Lateral root branching rather than main root thickening is generally pronounced in the case of hydroponically cultivated plants that make hydroponics unfit for the production of medicinal plants whose underground parts (roots, rhizome and stolon, *etc.*) are utilized. There are several reports on hydroponics of medicinal plants whose roots are utilized including *Bupleurum falcatum*[2] and *Glycyrrhiza glabra*.[3,4] However, productivity of hydroponically-cultivated *B. falcatum* roots was insufficient compared with the soil-cultivated ones[2] and hydroponically-cultivated *G. glabra* roots failed to accumulate sufficient active ingredients (not less than 2.5% of glycyrrhizic acid) as specified in the Japanese Pharmacopoeia.[5]

We succeeded in the production of crude drugs made from underground plant parts (roots and rhizome) with sufficient active ingredients as specified in the Japanese Pharmacopoeia[5] by using a novel hydroponics (Figure 2) for a year. Some of our works on hydroponics of medicinal plants are introduced but with special focus on *G. uralensis*.

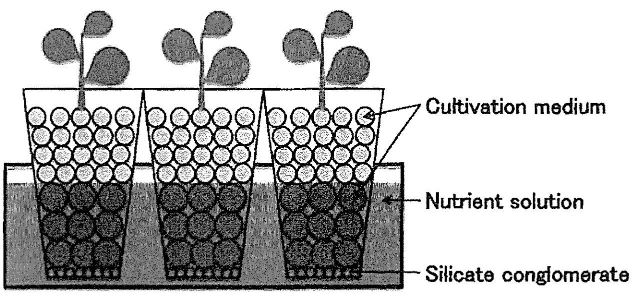

Figure 2 Hydroponics of medicinal plants whose underground parts are utilized

3. Production of glycyrrhiza by hydroponics of *G. uralensis*

Among crude drugs produced in China, glycyrrhiza as well as ephedra herb and pueraria root have been prepared from wild plants. Supply of medicinal glycyrrhiza used in Japan depends on wild *G. uralensis*.[6] Many field-cultivation studies have so far been done for stable and sufficient supply of glycyrrhiza.[6-10] Ozaki *et al.*[8,10] recently reported successful production of glycyrrhiza with performing over 5% glycyrrhizin by the selection of pharmaceutically fine strains and by their novel field-cultivation method of *G. uralensis* for a year using 10 cm diameter and 50 cm length plastic tube filled with compost. However, glycyrrhiza from a field-cultivated plant generally contains much less glycyrrhizin than that from a wild plant and most of field-cultivation studies[6,9] on *G. uralensis* reported that over 3 years of field-cultivation was required to obtain the esteemed crude drug (>2.5% glycyrrhizin) in The Japanese Pharmacopoeia.[5] In addition, field cultivation is amenable to unusual weather, natural disaster and artificial environmental disturbance by chemical pollutants and radioisotopes, *etc.*

Our Breeding and Physiology laboratory in Research Center for Medicinal Plant Resources (RCMPR), National Institute of Biomedical Innovation (NIBIO) preserves *in vitro* culture collections of tropical, subtropical, temperate and boreal medicinal plant species. Utilizing them, we are developing medicinal plants with new trait and efficient production system for pharmaceutically important secondary metabolites in the closed-type cultivation facilities. There were two *in vitro G. uralensis* plant strains when we launched hydroponics of medicinal plants whose underground parts are utilized. They were transplanted to soil in pots and cultivated in a closed-type greenhouse under constant growth environment (temperature, light cycle and relative humidity, *etc.*) to examine their growth and glycyrrhizin productivity. The results revealed that the strain that performed better in terms of root yield and glycyrrhizin productivity after one-year cultivation produced similar results after two- and three-years cultivation. In soil-cultivated *G. uralensis* roots, over a thousand days were required to obtain over 2.5% dry weight glycyrrhizin. There appeared high correlation between terrestrial stem yield and root yield (r^2=0.902) as well as between root yield and glycyrrhizin content (r^2=0.835). Therefore the *in vitro* plant strain that performed better root yield and glycyrrhizin productivity in the soil was selected and subjected to the further selection by shoot growth and shoot multiplication capability *in vitro*. Thus two subclones of *G. uralensis* were established. The micropropagated *in vitro* plant subclones were subjected to hydroponics in the closed-type greenhouse.

Among the cultivation medium tested in our hydroponics (Figure 2), promising results were obtained with the use of hydroball. The *G. uralensis* roots (diameter size > 1mm) harvested after 401 days hydroponic cultivation accumulated approximately 3% dry weight glycyrrhizin with small variation of value. Glycyrrhizin content in the roots of the same subclone reached 5.5% dry weight after 738 days of hydroponic cultivation.

4. Selection of *G. uralensis* clones suitable for hydroponics

Our RCMPR comprises 3 divisions including Hokkaido, Tsukuba and Tanegashima, and are preserving over 2,000 species and over 4,000 groups of medicinal and useful plants. *G. uralensis* are field-cultivating in Hokkaido and Tsukuba, and its seeds are produced in Hokkaido. Seeds of three *G. uralensis* strains harvested in Hokkaido were utilized to select pharmaceutically fine and productive clone for hydroponics. Three strains of *G. uralensis* plants germinated from seeds were subjected to hydroponics in the closed-type greenhouse. As observed in soil-cultivation in pots, the strain that performed the best root yield and glycyrrhizin content after a half-year cultivation also did after one-year cultivation though the data within the strain varied widely compared to the clonally propagated plants by *in vitro* culture. Thus one strain was selected and plants further germinated from the seeds of selected strain were subjected to hydroponics in growth camber (artificial lightning).

G. uralensis roots of the selected strain were harvested and analyzed their secondary metabolite contents after 4-month hydroball hydroponic cultivation. There were great variations of the data (yield and contents) among the clones and two promising clones were obtained (one clone performed 2.1% glycyrrhizin and another did 1.6% glycyrrhizin with the best root yield).

The selected *G. uralensis* clone (1.6% glycyrrhizin with the best root yield after 4 months hydroponics) clonally propagated by stolon cuttings demonstrated 3.1% dry weight glycyrrhizin together with 1.0% dry weight liquiritin, 0.10% dry weight isoliquiritin and 0.24% dry weight glycycoumarin within a year (353 days). Liquiritin in glycyrrhiza is one of the active ingredients that show antidepressant, antioxidant and neurotropic activities.[11)] It is reported that 2-year old *G. uralensis* roots field-cultivated by the use of plastic tube accumulated much less liquiritin than commercially available glycyrrhiza.[10)] On the other hand, the roots of our selected clone in hydroponics accumulated comparable liquiritin to the commercially available ones and relatively high glycycoumarin. Glycycoumarin in glycyrrhiza is also one of the active ingredients that act as a potent antispasmodic.[12)] Therefore our clone might be useful for Kampo formulation of shakuyakukanzoto that commonly being prescribed for cramp.

5. Development of artificial hydroponic system for glycyrrhiza

Our hydroponic studies of medicinal plants whose underground parts are utilized started in 2006 as a part of projects subsidized by Ministry of Economy, Trade and Industry, "Development of fundamental technologies for advanced manufacturing using plant biology: Development of fundamental technologies for production of high-value materials using transgenic plants", and by Ministry of Health, Labour and Welfare, Health Labour Sciences Research Grant, "Study on fundamental technology of stable preservation and effective utilization for medicinal plant resources". Development of artificial hydroponic system for glycyrrhiza has been launched since second half of 2008 as a joint research program within industry (Kajima Corporation), university (Chiba University, Department of Horticulture) and national research institute (RCMPR, NIBIO) on the basis of our precedential studies on hydroponics of medicinal plants including glycyrrhiza. Novel hydroponics device that differ from Figure 2 (Figure 3, without using culture medium) and *G. uralensis* plants suitable for

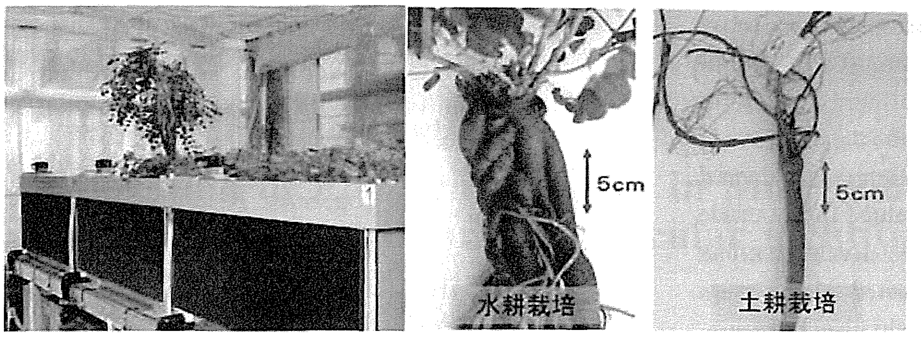

Figure 3 Novel hydroponics device for glycyrrhiza (left) and *G. uralensis* roots cultivated in hydroponics (center) and field (soil) (right) for 300 days (Photos: Kajima Corporation)

hydroponics have been invented in this project. The results of this study titled "Development of hydroponic cultivation system of licorice" was awarded Minister's Prize, the Ministry of Health, Labor and Welfare for the Industry-university-government cooperation meritorious person commendation on Sep. 22, 2011.[13)]

6. Efficient production of crude drugs made from plant underground part by hydroponics

Our hydroponics (Figure 2) was applied to belladonna (*Atropa belladonna*) and Japanese goldthread (*Coptis japonica*) as a part of the above mentioned project subsidized by Ministry of Economy, Trade and Industry, "Development of fundamental technologies for advanced manufacturing using plant biology: Development of fundamental technologies for production of high-value materials using transgenic plants". Clonally propagated *A. belladonna* and *C. japonica* plants by *in vitro* culture were subjected to hydroball-hydroponics and pumice sand-hydroponics, respectively.

A. belladonna is a perennial solanaceous medicinal plant mainly cultivated in Europe and USA[14)] and is not commercially cultivated in Japan. It contains alkaloids, the chief of which is hyoscyamine. Hyoscyamine has anticholinergic activity and used as a depressing drug for gastric secretion and gastrospasm. It is also used as eye drops for mydriasis and local anesthetic.[15)] *A. belladonna* roots hydroponically-cultivated for 6 months in the closed-type greenhouse accumulated over 0.4% dry weight hyoscyamine which matched the value in the Japanese Pharmacopoeia.[5)]

C. japonica is a perennial ranunculaceous medicinal plant grown in Asia, and its rhizome is used as crude drug, in which berberine is highly accumulated as the main alkaloid. Berberine shows strong antimicrobial activity toward both Gram-positive and -negative bacteria as well as other microorganisms.[16)] It has also been reported that berberine has beneficial effects on metabolic syndrome including blood cholesterol-lowering activity via upregulation of low-density lipoprotein receptor expression,[17)] anti-hypertension effects via induction of mobilization of circulating endothelial progenitor cells,[18)] and lowering of blood glucose level through increasing insulin receptor expression.[19)] Although various clinical trials of berberine for metabolic syndrome have been conducted,[17-19)] *C. japonica* is a slow-growing plant which requires over 5 years cultivation to obtain an esteemed crude drug matching the Japanese Pharmacopoeia (not less than 4.2% of berberine as berberine chloride). *C. japonica* rhizome hydroponically-cultivated for 6 months in the growth chamber accumulated over 7% berberine which is much higher than the ingredient value in the Japanese Pharmacopoeia. This value (over 7% dry weight berberine) of hydroponic *C. japonica* rhizome was comparable to the *C. japonica* rhizome field-cultivated for over 5 years. These two examples other than glycyrrhiza indicate our hydroponics is one of the promising tools for the production of crude drugs that is made from underground plant parts.

7. Future perspectives

Hydroponics of medicinal plants in the closed-type cultivation facilities is in one of the effective and promising solutions for sufficient and stable supply of high-value medicinal resources as mentioned above, especially for Japan which is the country with insufficient natural resources. However, its production costs are much more than that of field-cultivation because it needs the construction of specified facilities with additional running costs of electric, fuel, light and water charges, *etc.* Therefore to expand this technology in an economically feasible manner, cost reduction is an important issue to address.

There is no case of commercialization of crude drugs produced by hydroponics. Crude drugs prepared from wild resources are still highly valued inside crude drug and Kampo manufacture industry. Even the crude drugs prepared from the field-cultivated plants were compared with those prepared from wild plants pharmacologically and biopharmaceutically in the industry.[6] However, hydroponics of medicinal plants is an indispensable technology for the sustainable and sufficient supply, preservation, and prevention of medicinal resources from depletion with natural disaster and unexpected accident. It is our hope that our studies on hydroponics of medicinal plants will contribute to the sustainable supply of medicinal materials that promote and maintain Japanese health.

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2. Project of Research Center for Medical Plant Resources, National Institute of Biomedical Innovation, Japan

Dr. Nobuo KAWAHARA (National Institute of Biomedical Innovation (NIBIO); Japan)

Thank you Chairman. Good afternoon everybody. First of all, I would like to express my appreciation to Dr. Seki and all staff members of this symposium who gave me the opportunity of my presentation. Today, I would like to introduce the Project of Research Center for Medicinal Plant Resources, National Institute of Biomedical Innovation, Japan. So, my presentation is a little bit different from the standardization and regulation of medicinal plants, so please relax and enjoy hearing my presentation.

#2
So, this is today's contents. At first, I would like to tell you about introduction of research center and outline of our database system. Then, I would like to show you a construction of integrated information database of medicinal plants using for Kampo medicines, and as our project.

#3-4
At first, I would like to introduce our research center. Research Center for Medicinal Plant Resources, formerly Medicinal Plant Research Station of National Institute of Health Sciences, replaced as the section of National Institute of Biomedical Innovation from April 2005. The Research Center for Medicinal Plant Resources, the only comprehensive research center in Japan for medicinal plants performs research and development on technology relative to the cultivation and breeding of medicinal plants, and chemical and biological evaluations and cultivates and preserves more than 4,000 species and groups of medicinal plants at three divisions; Hokkaido, and Tsukuba, and Tanegashima, and Wakayama Branch.

#5
And, this slide shows the collection of plants and seeds in Tsukuba, and Hokkaido, and Tanegashima Division, and Wakayama Branch.

#6
And, also this slide shows the building for the conservation of medicinal plant resources and it contains samples of crude drugs, herbarium specimen and seeds. Especially, more than 13,000 seeds are preserved under various temperatures.

#7
This slide shows the building for the researches on the medicinal plant resources. We have more than 180 species in vitro culture and perform the chemical and biological evaluations and conduct research using biotechnology and genetic technology while serving as the main facility of the research center.

#8-9
Next, I am going to introduce our medicinal plant database. This slide shows the purpose of construction of medicinal plant database to ensure the quality of medicinal plant resources. We invest resources and with a higher value by adding information. According to our semi-long-term objective, first 5 years, 2005 to 2009, collect and preserve medicinal plant resources aggressively and deal with administrative request precisely. So, we tried to construct a database on most important 100 species of medicinal plants we have in our institute, in which their characteristics, ingredients, and physiological activities.

#10
This slide shows the invest resources with higher value by adding information, namely, the value of the medicinal plant resources become higher with additional information.

#11
This slide shows the fundamental structure of MPDB. This database constructed mainly in three parts; information on growth and cultivation, basic information on plants, and information on crude drugs.

#12
This slide shows the brief introduction of MPDB. Top page shows the keyword selection, plant name, and crude drug name, and English name. Now, we showed example database, search source of the crude drugs, and natural sweetener and Chinese licorice, Kanzo.

#13
This slide shows the search result plant name hit list and detailed information of Glycyrrhiza uralensis.

#14
This slide shows the morphology, habitats, and climate preference of Glycyrrhiza uralensis.

#15
This slide shows the photo library from seeds to crude drugs.

#16
Also, if you search crude drug name by keyword "Kanzo," the result of crude drug search shows the Kanzo list of hit plants.

#17
This slide shows the detailed information of the crude drug Kanzo and Kampo formulae that contain Kanzo.

#18
This slide shows the characteristics and advantage of our database. It covers information on more than 100 species of medicinal plants. Only one database, that information on plants and crude drugs are linked. It files detailed information for cultivation, up to 1,300 photos, and it is easy to access, and it is able to handle data intuitively as a whole network. This database was released on March 31st, 2010.

#19
So, third topic is the construction of "Integrated Information Database of Medicinal Plants Using for Kampo Medicines (IIDMP)." This research project began by supporting a Health and Labour Sciences Research Grant from April 2010.

#20
In this project, we have two major purposes, thorough construction of integrated information database of medicinal plants using for Kampo medicines. First, the viewpoint of administration, provision of useful information for quality control, safety and cultivation promotion of the medicinal plants. Second, viewpoint of research support, contribution for research of biological resources and industrial promotion of Kampo medicines.

#21
This slide shows the method of this project. We select about 75 kinds of crude drugs, including 44 important ethical Kampo extract formulations that account for about 90% of Kampo extract products mainly compose the database. Registration of various information into database, then we will disclose this database on the website of National Institute of Biomedical Innovation. In this year, we select five core crude drugs; Atractylodes Lancea Rhizome, and Ginger, Ginseng, Glycyrrhiza and Scutellaria Root, and plan to collect various information data from these crude drugs. Then, next 15 important crude drugs are also nominated.

#22
This slide shows the fundamental structure of IIDMP, and chemical analysis information, sensory test data, internal structure of crude drugs, herbarium specimens, resource management, management of plant and seed materials, and genetic discrimination, discrimination of plant origin by genetic information, in vitro culture information, efficient propagation method, cultivation information, efficient production method, crude drug extract, physiological activity, adverse effect information, and Kampo formulae information are newly adopted.

#23
This slide shows the research system of this project. Research Center for Medicinal Plant Resources, these are associate laboratories and also research cooperators, cooperate each other.

#24
This slide shows the yearly plan of database project from 2010. First year, construction of database system and also collection and accumulation of various information data, then from the second year, input of various information data into database and we will disclose the database until the end of third year.

#25
So, this is the fourth topic, Hydroponic Cultivation of Medicinal Plant in the Closed-type Plant Factory.

#27
This slide shows the circumstances around Glycyrrhiza uralensis, its supply still depends on collection of the wild plants in the north-western region of China. Recently, China fortifies the control of collection to prevent the desertification. Some research groups have started field cultivation of Glycyrrhiza, however, over 3 years cultivation is required to obtain esteemed crude drug over 2.5% Glycyrrhizin. These circumstances mean insufficient supply of Glycyrrhiza to satisfy constant and increasing demand.
One of the solutions of the hydroponic cultivation of medicinal plant in the closed-type plant factory, this system enables us to control and maintain the optimal environmental conditions to supply well-identified, and high-quality medicinal plants stably, to prevent environmental pollution by agrochemicals, and to contain transgenic genes in the case of transgenic plants. Therefore, this system contributes a safe and stable supply of medicinal plant resources.

#28
When we started our hydroponic cultivation study of Glycyrrhiza uralensis, we had two in vitro plant strains, named GuH and Gu, and these two strains were subjected to soil cultivation in closed-type greenhouse to examine their growth and Glycyrrhizin productivity.
After a year, we found Gu strain was superior both in the root growth and Glycyrrhizin production and it was selected for hydroponic cultivation study. Generally, liquid float hydroponics is commercially practiced for leaf vegetables. However, it is not preferable to get thick roots which are desirable morphology for crude drug. Therefore, we invented the hydroponic system for the root growth and underground part of the plant is settled in cultivation medium such as Cocopeat and Hydroball. Nutrient solution provided to the root by the capillary of the cultivation medium. Patent application of this cultivation system for medicinal plants was submitted to the Japan Patent Office.

#29
Two Gu sub-clones, Gu2-2-1 and Gu2-3-2, that micropropagated through tissue culture were used for the experiment. During the study we found that cocopeat hydroponics was not suitable for Glycyrrhiza, in contrast the plant grew where the thickened Glycyrrhiza root, its photo is here, were obtained after 400 days in hydroponic cultivation. This figure shows the Glycyrrhizin concentration

in roots, soil cultivated for around 1,000 days and hydroponically cultivated for around 400 days, as seen in the figure the roots hydroponically cultivated only for 400 days accumulated around 3% Glycyrrhizin.

#32
This is the final topic, Research on Antileishmanial Compounds from Medicinal Plant Resources.

#33
Firstly, I would like to discuss the topic, why are the plant resources important? As you know, the drug discovery was recently seen some big changes with the introduction of new techniques such as genomic drug discovery and these have already become mainstream techniques. Accordingly, many methods that utilize plant resources for drug development have become obsolete.
However, in modern drug discovery techniques such as "combinatorial chemistry" and "high-throughput screening", low-molecular weight synthetic compounds have been regarded as skeletal limitations of their respective chemical structures. This reminds us of the importance of naturally-occurring compounds, especially those of plant origin.
Plants have the ability to biosynthesize the compounds with unique chemical structures and most of these compounds cannot be synthesized even today. Medicinal plants are used as folk medicine in most countries. So, on the basis of such traditional experiences we think that there is a high possibility of discovering new medicines from the medicinal plant resources.

#34
Next, what is leishmaniasis? Leishmaniasis is an infectious disease distributed mainly in tropical regions, and most countries affected are developing countries. Leishmaniasis is transmitted by small sand fly and classified into three clinical conditions according to Leishmania strain. The first is the cutaneous type where ulcers occur in the affected area. The second is mucocutaneous type, which results in inflammation of the nasal and oral mucosa. The third is the visceral type and is the most serious of the three types.
Maybe you know, recently it is very serious pandemic at the southern part of Sudan, Africa. This pandemic is this type. So, infection causes inflammation of the liver and the spleen and the condition is fatal if left untreated. Treatment, however, is not that simple, because there are some problems with antileishmanial drugs currently available. For example, existing treatments such as pentavalent antimonials are expensive and highly toxic and require a long-term administration. Furthermore, expensive drugs are out of reach to most patients in developing countries.

#35
Leishmaniasis currently affected 12 million people across 88 countries, and South America in particular, all type of leishmaniasis are distributed. Especially in Peru, many people have suffered from this disease since ancient times. About 10 years ago, Peruvian researchers asked us to find a new treatment derived from the medicinal plants in Peru, this is why we started this project.

#43-44
This slide shows the antileishmanial activity of crude drugs used in Kampo medicines prescription. In addition to screening mentioned so far, we have also screened the antileishmanial activity of crude drugs used as Kampo medicine prescriptions. During the screening of several crude drugs used in Kampo, the hexane extract of Lithospermum root shows the highest active result. The Lithospermum root is well known to contain the shikonin and several of its derivatives from the purple pigment. This showed extremely potent activity.

#45
Lithospermum root is one of the ingredients of the Kampo ointment shi-un-ko which is a very famous ointment for the treatment of various external diseases and it is especially effective for treating the burns.

#46
We discovered the potent antileishmanial activity of shikonin derivatives in Lithospermum root, then set out to conduct a clinical study in cooperation with local doctors. Clinical trial test was conducted with the patients of various ages in specific region in Peru. All patients had cutaneous leishmaniasis.

#47
This table summarized the community areas where clinical tests were conducted. Four areas were selected for clinical test and 53 patients were subjected to tests for shi-un-ko.

#48-50
Here, we can see lesions of patients in the clinical trial. Shi-un-ko ointment was applied to the skin lesion of the cutaneous leishmaniasis. This shows the biopsy of the affected areas after scar formation. As seen here, the entire affected area formed the scar tissue after treatment with shi-un-ko.

#51
This table summarized the clinical tests performed in Peru. In 46 patients, a scar formed in 1 month, and protozoa survival was not observed in any cases in biopsy after treated. Andean-type leishmaniasis normally healed spontaneously in 6 months to 1 year, but with shi-un-ko ointment the healing time was reduced to 1 month.

#52
Here is my summary. In our research for antileishmanial compounds from plants, based on information of local folk medicine. Several active ingredients were isolated and their chemical structures were elucidated. It was in fact the potent antileishmanial activity of shikonin that led us to conduct clinical trials with the Kampo ointment "Shi-un-ko", which we found to be effective against cutaneous leishmaniasis. Moreover, this ointment can be applied to patients, who no longer respond to existing drugs and even to pregnant women. Thank you for your kind attention.

4-2

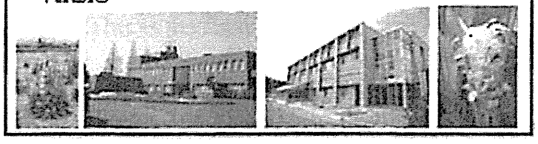
Project of Research Center for Medicinal Plant Resources, National Institute of Biomedical Innovation, Japan

Tokyo Forum on International Standardization of Natural Medicines

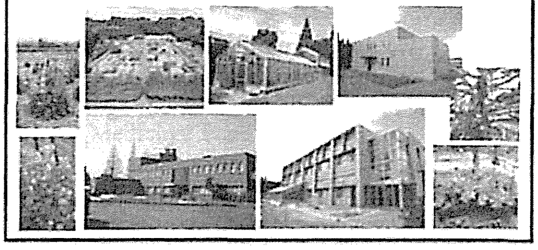
Nobuo KAWAHARA

Research Center for Medicinal Plant Resources, National Institute of Biomedical Innovation

NIBIO RCMPR



1. Introduction of Research Center for Medicinal Plant Resources (RCMPR), National Institute of Biomedical Innovation



Contents

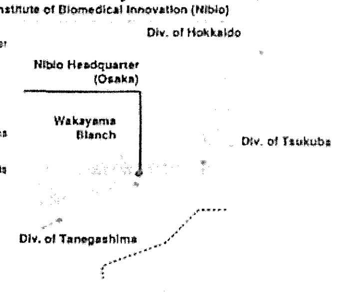
Research Center for Medicinal Plant Resources, At a Glance

Formerly Medicinal Plant Research Station of NIHS (Ministry of Health, Labor and Welfare)

From Apr. 2005 Subsection of Biological Resource Division, National Institute of Biomedical Innovation (Nibio)

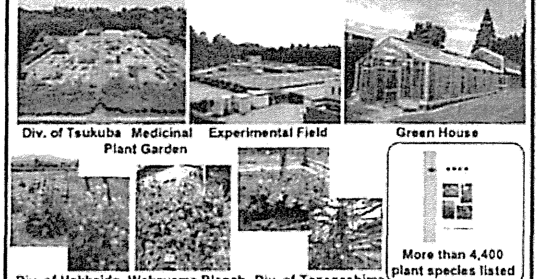
Medicinal Plant Resources

- Collection, preservation, transfer
- Development of cultivation and preparation technique
  - Domestic cultivation
  - Breeding of superior cultivars
- Exploitation of unused resources
- Development of molecular breeding & propagation methods
- Creation of superior phenotype
  - Genetic transformation
- Ultra-long-term preservation
  - Ultra-low-temp. preservation
- Utilization of "plant factory"

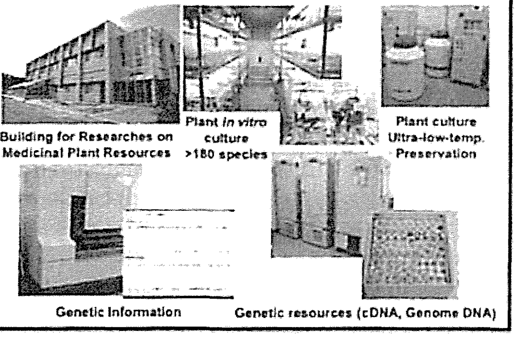


Medicinal Plant Resources of RCMPR

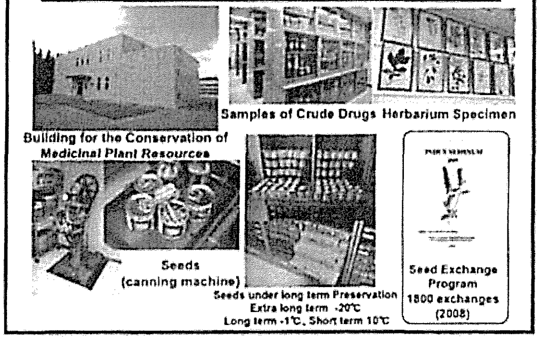
Collections of Plants (vegetative stage) and Seeds



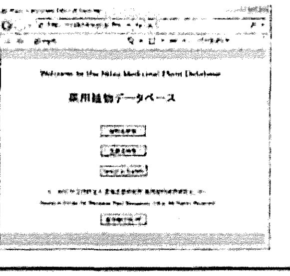
Medicinal Plant Resources of RCMPR



Medicinal Plant Resources of RCMPR



2. Introduction of Medicinal Plant Database (MPDB)



Purpose of Construction of Medicinal Plant Database (MPDB)

Medicinal plant resource collection. Value of "resource" itself is limited. To ensure the "quality" of resources…

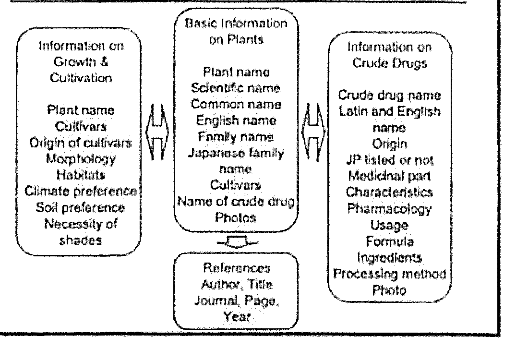
Invest "resources" with "higher value" by adding "information".

Research Center of Medicinal Plant Resources
(One of) Our semi-long-term Objective (First 5 years, 2005 to 2009)
"Collect and preserve medicinal plant resources aggressively, and deal with administrative request precisely."

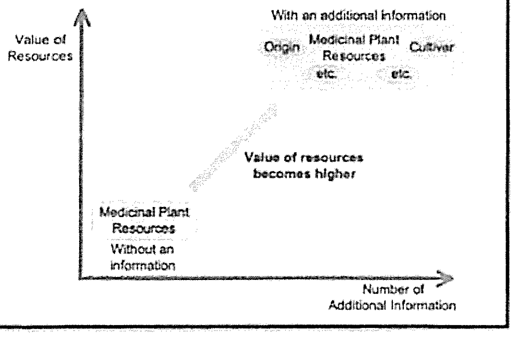
Semi-long-term Project (First 5 years, 2005 to 2009)
"Construct a database on most important 100 species of medicinal plants we have in our institute, in which their characteristics, ingredients and physiological activities are filed."

Construction of MPDB
All divisions of RCMPR worked together
Data collection on most important 100 species of medicinal plants

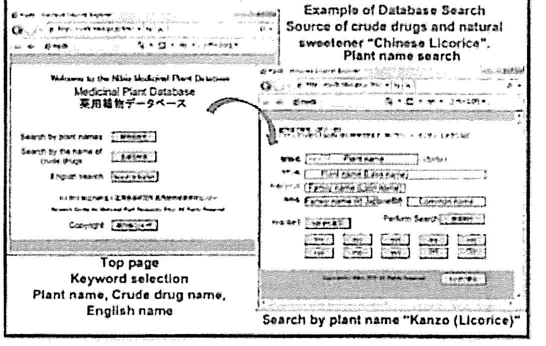
Fundamental Structure of MPDB



Invest "Resources" with "Higher Value" by Adding "Information"



Brief Introduction of RCMPR MPDB



Detailed information on *Glycyrrhiza ularensis*

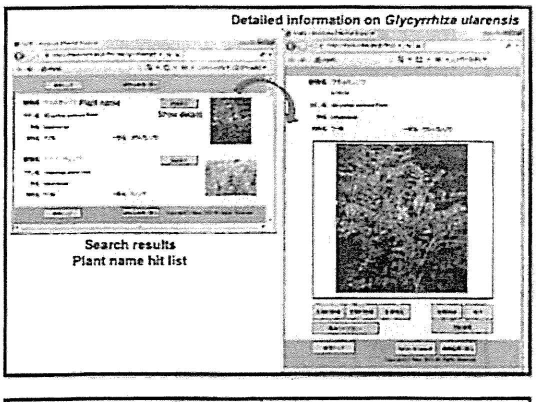
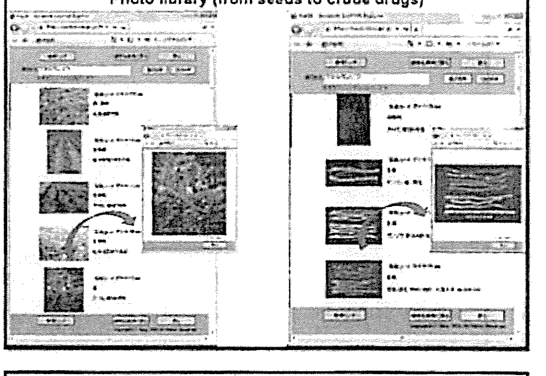
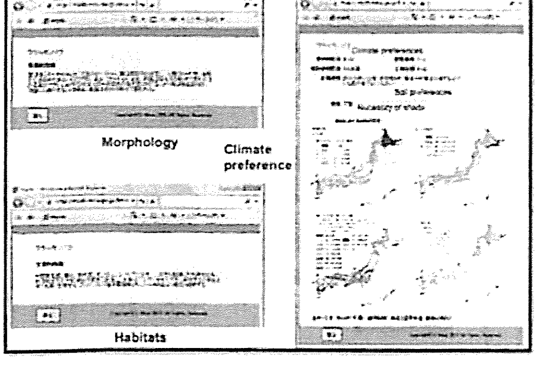
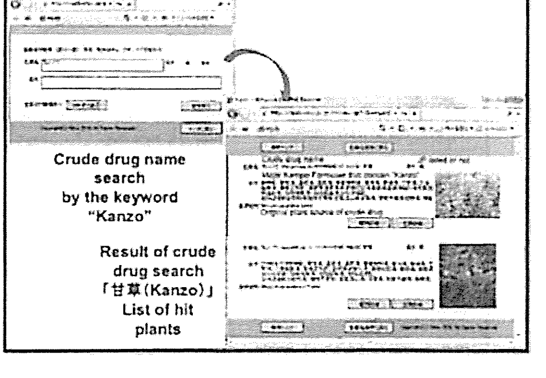
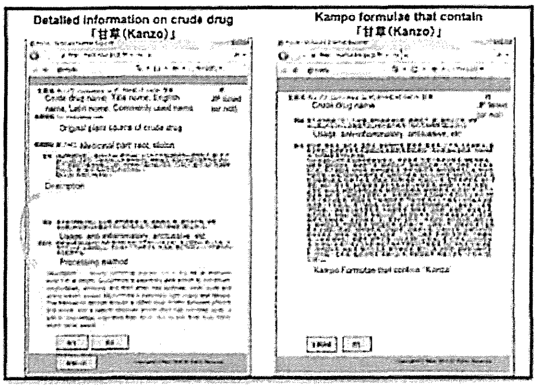


Photo library (from seeds to crude drugs)





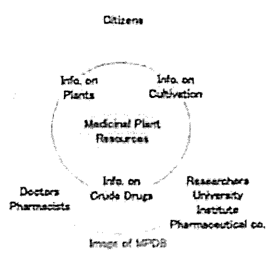




3. Construction of "Integrated Information Database of Medicinal Plants Using for Kampo Medicines (IIDMP)"

This research project began by supporting a Health and Labour Sciences Research Grant from April 2010.

Research Center for Medicinal Plant Resources (RCMPR) Medicinal Plant Database (MPDB)



Advantages
- Covers information on more than 100 species of medicinal plants.
- Only one database that information on plants and crude drugs are linked.
- Detailed information for cultivation is filed.
- Up to 1,300 photos filed.
- Easy to access.
- Able to handle data intuitively as a whole network.

Released on Mar 31, 2010.
http://www.nibio.go.jp/, http://wwwts9.nibio.go.jp/
No ID, password required.

Integrated information database of medicinal plants using for Kampo medicines

Our two major purposes

Through construction of integrated information database of medicinal plants using for Kampo medicines

1. Viewpoint of administration
Provision of useful information for quality control, safety and cultivation promotion of the medicinal plants

2. Viewpoint of research support
Contribution for research of biological resources and industrial promotion of Kampo medicines

Integrated information database of medicinal plants using for Kampo medicines

Method
- About 75 kinds of the crude drugs including 44 important ethical Kampo extract formulations that account for about 90% of Kampo extract products mainly compose the database.
- Registration various information into database.
- Disclosing of database on the web site of National Institute of Biomedical Innovation.

In this year, we select 5 core crude drugs (Atractylodes Lancea Rhizome, Ginger, Ginseng, Glycyrrhiza and Scutellaria Root) and plan to collect various information data from these crude drugs. Then next 15 important crude drugs are also nominated.

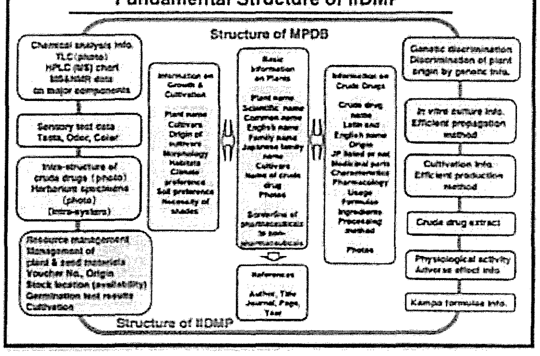
Research system

Main laboratories
Research Center for Medicinal Plant Resources, National Institute of Biomedical Innovation
Hokkaido div. Tsukuba div. Tanegashima div.

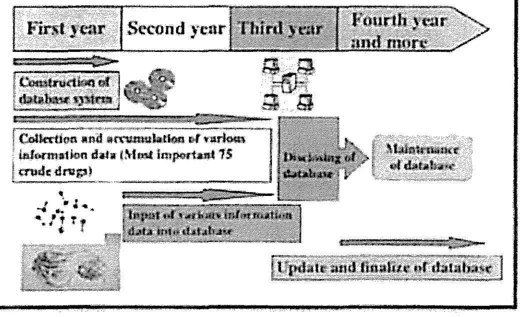
Associate laboratories
National Institute of Health Sciences
Institute of Natural Medicine, University of Toyama
Kanazawa University
Gifu College of Pharmacy
Faculty of Pharmaceutical sciences, Keio University

Research cooperators
Pharmaceuticals and Medical Devices Agency
Japan Kampo Medicines Manufacturers Association
Tokyo Crude Drugs Association
Japan Reagent Association etc.

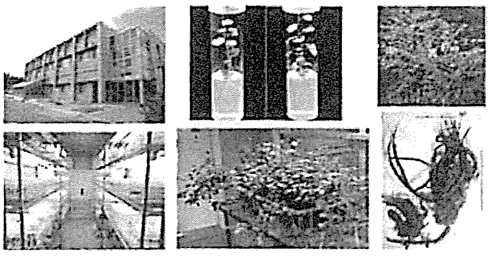
Fundamental Structure of IIDMP



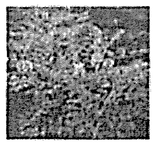
Yearly plan of database project from 2010



4. Hydroponic Cultivation of Medicinal Plant in the Closed-type Plant Factory



Circumstances around *Glycyrrhiza uralensis*



- Its supply still depends on collection of the wild plants in the north-western region of China and wild resources with good quality are decreasing.
- People's Republic of China fortifies the control of collection to prevent desertification.
- Over 3 years field-cultivation is required to obtain esteemed crude drug (>2.5% glycyrrhizin in The Japanese Pharmacopoeia).

↓

Insufficient supply of glycyrrhiza to satisfy constant and increasing demand

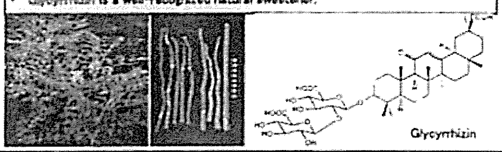
↑

Hydroponic cultivation of medicinal plant in the closed-type plant factory
- It enables us to control and maintain the optimal environmental conditions.
  - to supply well-identified and high-quality medicinal plants stably.
  - to prevent environmental pollution by agrochemicals.
  - to contain transgenic genes (in the case of transgenic plants)

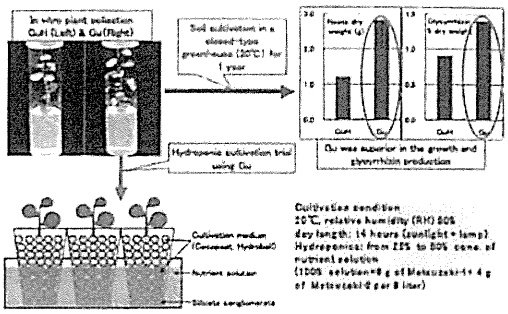
→Safe and stable supply of medicinal plants

Glycyrrhiza uralensis (Chinese licorice)

- *Glycyrrhiza uralensis* is perennial Leguminosae (Fabaceae) family and native to northeast, northcentral and northwest China and Mongolia.
- Glycyrrhiza (root & stolon) is most frequently prescribed crude drug in Kampo formulae (traditional Japanese medicine) and serves as the principal and supporting drug.
- Glycyrrhiza is a well-known drug used as a remedy for inflammatory, allergic and gastric disorders.
- Glycyrrhizin (one of the active principles) extracted from glycyrrhiza is used as curatives for chronic liver and allergic diseases
- Glycyrrhizin is a well-recognized natural sweetener.



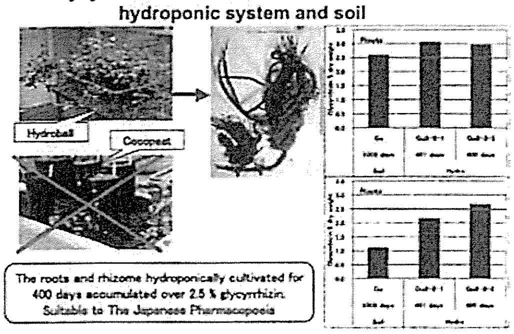
Establishment of hydroponic cultivation system for *G. uralensis*



Cultivation condition
20℃, relative humidity (RH) 60%
day length: 14 hours (sunlight + lamp)
Hydroponics: from 25% to 50% conc. of nutrient solution
(100% solution=8 g of Matsuzaki-1+4 g of Matsuzaki-2 per 8 liter)

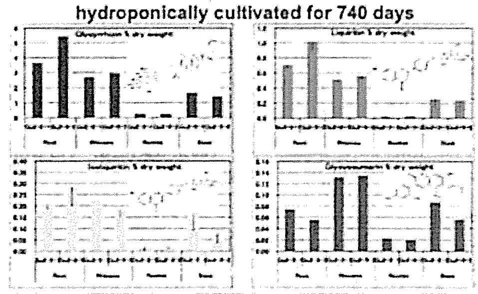
Patent application for hydroponic cultivation of medicinal plants was submitted to the Japan Patent Office

Glycyrrhzin accumulation of *G. uralensis* in hydroponic system and soil



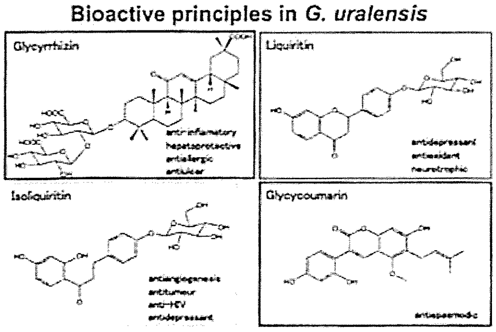
The roots and rhizome hydroponically cultivated for 400 days accumulated over 2.5 % glycyrrhizin.
Suitable to The Japanese Pharmacopoeia

Bioactive compounds in *G. uralensis* hydroponically cultivated for 740 days

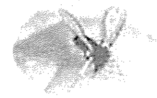


Non-transformed *G. uralensis* clone Gu2-3-2 accumulated 3.5% glycyrrhizin together with liquiritin, isoliquiritin and glycycoumarin in its roots after 740 days of hydroponic cultivation.

Bioactive principles in *G. uralensis*



5. Research on Antileishmanial Compounds from Medicinal Plant Resources



NIBIO National Institute of Biomedical Innovation

RCMPR Research Center for Medicinal Plant Resources