pharma dermocosmetics

DOCUMENTAZIONE SCIENTIFICA

DOCUMENTAZIONE RISERVATA ALLA CLASSE MEDICA

maca Repair

Relazioni Scientifiche

Lepidium meyenii (Maca) nel trattamento della Calvizie

Stato dell'arte

La perdita dei capelli , generalmente può non considerarsi una malattia, anche se è risaputo condizionare psicologicamente una persona che ne soffre quindi, incidere sulla sua qualità della vita. Le cause principali della caduta dei capelli sono di origine alimentare, atmosferica, dovute allo stress psico-fisico. Se si considera che la perdita da 50 a 100 capelli ogni giorno, è ritenuta normale (fisiologico), bisogna sottolineare che il primo "campanello d'allarme" verso la condizione di calvizie è la perdita di capelli superiore alla cifra succitata. Per non andare incontro a calvizie pertanto, è necessario che tutti i capelli persi siano sostituiti. I capelli caduti, non ricrescono sempre poiché, in taluni casi, la matrice pilifera sostituisce il capello "morto" con uno di calibro nettamente inferiore ovvero può non sostituirlo affatto: in questo caso si ha a che fare con alopecia la cui entità dipende dal disegno assunto dalle aree che si sono sfoltite. La normale caduta fisiologica dei capelli aumenta nelle stagioni di transizione (autunno-primavera) perché l'uomo conserva una manifestazione ancestrale propria di altri mammiferi pelosi: la muta. Nei periodi da aprile a maggio e da settembre a novembre, alcuni ormoni attivano un processo sincronizzato di caduta: Si tratta di un fatto fisiologico che non è causa di calvizie definitiva[1]. La caduta dei capelli può dipendere anche dallo stress: condizioni psicofisiche difficili, soprattutto se prolungate, possono provocare, infatti, un aumento della caduta dei capelli, talora anche molto pronunciato. Altre cause sono gli shock emotivi, i periodi di super-attività (studio, responsabilità professionali, difficoltà familiari, problemi di relazione, ecc.), attività sportive o professionali faticose e non associate a regimi alimentari compensativi e malattie debilitanti[2]. Anche i farmaci, possono provocare la caduta dei capelli: alcuni medicinali hanno dimostrato di provocare una perdita di essi, ed in particolare alcune classi di antitumorali e di antidepressivi possono causare l'ingresso di un

[1] Ross, E.K. and Shapiro, J. (2005) Management of hair loss. Dermatol. Clin. 23, 227–243
[2] Dawber, R., ed. (1997) Diseases of the Hair and Scalp, Blackwell

alto numero di capelli in fase telogen e influenzarne la caduta[3]. Con la sospensione della terapia farmacologica il ciclo pilifero, generalmente riprende il suo andamento fisiologico anche se è consigliabile "aiutare" i capelli con prodotti nutrienti e rinforzanti soprattutto se la malattia è stata debilitante. Quando si interviene sulle cause della perdita dei capelli con trattamenti locali e, se necessario, con cure adeguate, è possibile riportare le condizioni alla normalità in un tempo relativamente breve con elevate probabilità di successo. L'alopecia androgenetica (AGA), che colpisce un gran numero di uomini e donne, è il tipo più comune di perdita dei capelli. AGA può verificarsi già nell'adolescenza, ma di solito si manifesta in età adulta[4]. Essa colpisce almeno la metà di tutti gli uomini con età media di 50 anni, e raggiunge il 70% nelle persone con età media di 70 anni . AGA è un disturbo androgeno-dipendente e geneticamente acquisito, causato da eccessiva attività dell'enzima 5-alfa-reduttasi nel follicolo pilifero da una eccessiva concentrazione di ormoni maschili che si trasformano in testosterone (isoenzima di tipo 1: promuove la reazione a livello della ghiandola sebacea; isoenzima di tipo 2: agisce a livello della prostata e del follicolo pilifero). la 5-alfa-reduttasi, infatti, converte il testosterone in un ormone androgeno diidrotestosterone (DHT) che riesce ad agire sul DNA, determinando un aumento della produzione sebacea e l'inibizione della sintesi proteica delle cellule germinative dei capelli[5].

Trattamenti della Calvizie

Nonostante molte persone affette da calvizie androgenetica scelgono di accettare la loro condizione, esistono numerosi trattamenti efficaci capaci non solo di ridurre ed arrestare la perdita dei capelli ma anche di stimolarne la ricrescita. Nel trattamento dell'alopecia androgenetica si possono distinguere due differenti trattamenti: quelli farmacologici e quelli cosmetici. In entrambi i casi l'efficacia è condizionata da fattori soggettivi, tra i quali il sesso, l'età, e lo stadio evolutivo del problema.

[3] Olsen, E.A. et al. (2005) Evaluation and treatment of male and female pattern hair loss. J. Am. Acad. Dermatol. 52, 301–311
[4] Sinclair, R.D., 2004. Male androgenetic alopecia. Journal of Men's Health and Gender 1, 319–327.
[5] Trüeb, R.M., 2002. Molecular mechanisms of androgenetic alopecia. Experimental Gerontology 37, 981–990.

I farmaci utilizzati per tale disordine sono essenzialmente due la finastaride ed il minoxidil. Il farmaco più importante è sicuramente la **finasteride**. La finasteride, data la sua capacità di inibire la 5-alfa riduttasi, è una sostanza usata per il trattamento dell'ipertrofia prostatica benigna. Il problema maggiore dell'utilizzo della finasteride per il trattamento contro la caduta dei capelli insorge al momento in cui si decide di interrompere la cura: nei mesi successivi, infatti, i capelli riprenderanno a cadere ed una nuova terapia non consentirebbe uguali benefici. Sono associati alla cura con Finasteride alcuni effetti collaterali (risolvibili comunque con la sospensione del farmaco) tra i più evidenti: diminuzione del desiderio sessuale, minore concentrazione di spermatozoi nel liquido seminale, etcc[6].

Altro farmaco molto utilizzato è il **minoxidil,** già noto per la cura dell'ipertensione. Anche se non si conosce bene il meccanismo di azione, sembra che la sua efficacia sia riconducibile alla stimolazione del bulbo pilifero. Anche in questo caso, l'uso deve essere continuativo, perché la sospensione riporta i capelli alla situazione iniziale precedente la terapia. I principali effetti collaterali sono: ipotensione, infiammazioni, arrossamenti, prurito[7].

Rimedi Naturali - Lepidium meyenii (Maca)

Negli ultimi anni la ricerca scientifica si è concentrata sullo studio di nuovi attivi di origine naturale, efficaci nell'eliminare o ridurre l'alopecia androgenetica e/o calvizie comune e aventi effetti collaterali blandi o pressoché nulli. Molti studi in Europa e negli Stati Uniti hanno rivelato che alcuni le piante, come la Serenoa repens, hanno la capacità di inibire la 5 alfa reduttasi (5R). Questa pianta possiede bacche dalle quali si ottiene un fitoderivato ad attività antiandrogena, quindi capace di ridurre la produzione del deidrotestosterone. La serenoa Repens agisce per via generale ed il suo effetto è simile a quello della finasteride; gli studi sul suo effetto anticalvizie ed

[6] Abramowicz, M., 1998. Propecia and rogain extra strength for alopecia. The MedicalLetter 40, 25–27.
[7] Messenger, A.G. and Rundegren, J. (2004) Minoxidil: mechanisms of action on hair growth. Br. J. Dermatol. 150, 186–194

antiseborroico sono abbastanza recenti mentre esistono da tempo in commercio farmaci e integratori a base di serenoa repens per il trattamento e la prevenzione dell'ipertrofia prostatica[8].

Molti Studi pertanto hanno indicato che le piante o sostanze con attività verso la 5R sono capaci di stimolare anche la ricrescita. La corteccia dell'albero del "Corbezzolo Cinese "[9], i semi del cedro bianco[10], l'estratto delle foglie della pianta del pepe nero[11] , e l'epigallocatechina-3-gallato (EGCG) trovato nel tè verde[12] sono tutti esempi di come si possa promuovere la crescita dei capelli con attività riconducibili sia all' inibizione dell'enzima 5 R o all'aumento della vitalità delle cellule epiteliali.

Recentemente, nel campo cosmetico e nutraceutico, la comunità scientifica si è molto interessata allo studio di un pianta erbacea annuale, nativa della Cordigliera delle Ande del Perù e della Bolivia: Lepidium meyenii comunemente nota con il nome di **Maca**. Questo tubero, famoso per la sua radice commestibile, è da sempre utilizzato dalle popolazioni andine come ricostituente, per la fertilità maschile e come rimedio dei sintomi della menopausa. A questo punto sembrerebbe naturale chiedersi : " ma quali sono le sostanze bioattive presenti nella **Maca**?".

A questa domanda la comunità scientifica ha risposto con una corposa documentazione che essenzialmente si può riassumere in poche parole: La Maca presenta numerose sostante bioattive !

I numerosi studi effettuati confermano, infatti, che la Lepidium Meyenii è ricca di flavonoidi, selenio, e numerosi polifenoli che conferiscono una spiccata attività antiossidante[13].

Sulla base dei dati raccolti, quindi, La **Maca** comincia ad essere utilizzata come integratore alimentare o supplemento in tutti i casi di astenia e nel trattamento della sindrome da fatica

[8] Niederprûm, H.J., Schweikert, H.U., Zânker, K.S., 1994. Testosterone 5-reductase inhibition by free fatty acids from Sabal serrulata fruits. Phytomedicine 1,127–133

[9] Matsuda, H., Yamazaki, M., Naruto, S., Asanuma, Y., Kubo, M., 2002. Anti-androgenic and hair growth promoting activities of Lygodii spora spore of Lygodium japonicum) I. Active constituents inhibiting testosterone 5_-reductase. Biological and Pharmaceutical Bulletin 25, 622–626

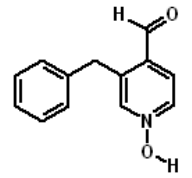
[10] Park, W.-S., Lee, C.-H., Lee, B.-G., Chang, I.-S., 2003. The extract of Thujae occidentalis semen inhibited 5-reductase and adrochronogenetic alopecia of B6CBAF1/j hybrid mouse. Journal of Dermatological Science 31, 91–98.

[11] Hirata, N., Tokunaga, M., Naruto, S., Iinuma, M., Matsuda, H., 2007. Testosterone 5_-reductase inhibitory active constituents of Piper nigrum leaf. Biological and
Pharmaceutical Bulletin 30, 2402–2405

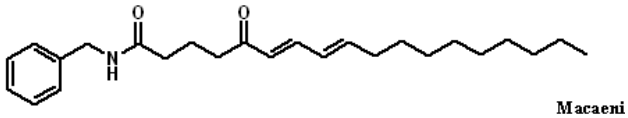
[12] Esfandiari, A. and Kelley, P. (2005) The effects of tea polyphenolic compounds on hair loss among rodents. J. Natl. Med. Assoc. 97, 816–818

[13] Rond´an-Sanabria GG and Finardi-Filho F, Physical–chemical and functional of maca root starch (*Lepidium meyenii* Walpers). *Food Chem* **114**:492–498 (2009).

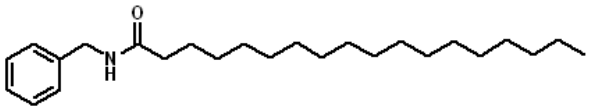
cronica[14]. Negli USA, è anche utilizzata come supplemento per diverse disfunzioni sessuali negli uomini e nelle donne. L'attività "afrodisiaca" di Lepidium meyenii è riconducibile alla presenza non solo dei polifenoli ma sopratutto ad alcune nuove classi di composti, definite con i seguenti nomi: macaridine, macamidi e macaeni[15].



Macaridine



Macaeni

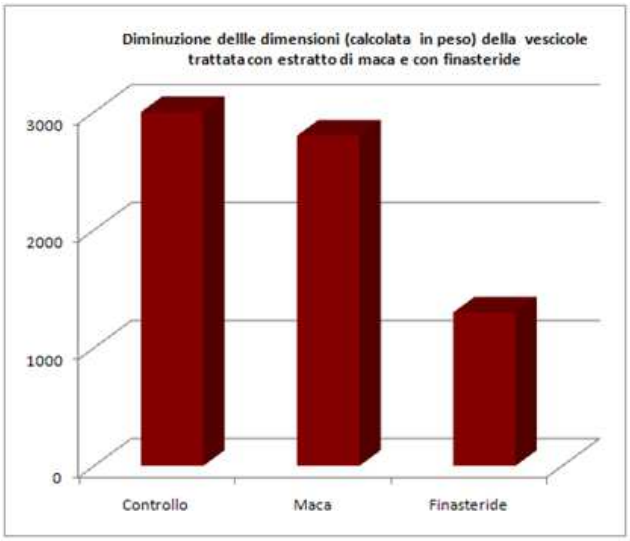


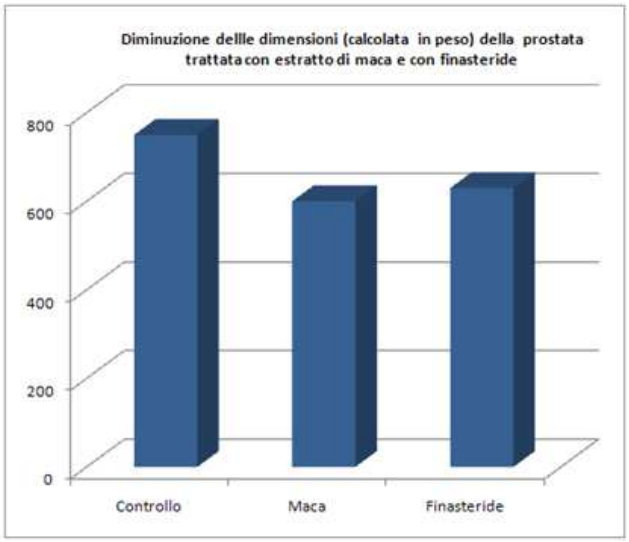
Macamidi

Numerosi studi riportano la positiva risposta di estratti acquosi della Maca all'ipertrofia prostatica benigna e i vantaggi rispetto alle terapie farmacologiche a base di finasteride[16].

Le conclusioni che si possono trarre da tali lavori scientifici sono che la Maca è una valida altenativa ai trattamenti classici; non altera (diminuizione) i valori di testosterone nel sangue, quindi della libido (desiderio sessuale) e della risposta erettile.

[14] Valentova´ K, Ulrichova´ J. Smallanthus sonchifolius and Lepidium meyeniiVprospective Andean crops for the prevention of chronic diseases. Biomed Papers 2003;147:119/130.
[15] Muhammad I, Zhao J, Dunbar DC, Khan IA. (2002) Constituents of Lepidium meyenii 'maca'. Phytochemistry *59*, 105–10
[16] Gasco M, Villegas L, Yucra S, Rubio J, Gonzales GF (2007) Effect dose–response of red maca on benign prostate hyperplasia in male rats. Phytomedicine 14:460–464.





Da un punto di vista biochimico, l'estratto di Maca, riesce ad inibire la 5 alfa reduttasi analogamente alla finsteride, e diversamente da questa interviene solo sulla prostata e non sulle ghiandole seminali. Sulla base di tali studi, di inibizione enzimatica, ovviamente risulta normale domandarsi se l'estratto di Maca abbia una qualche attività sulla calvizie[17].

E' ragionevole considerare la Maca una reale alternativa ai trattamenti farmacologici; essa infatti, essendo ricca di molti polifenoli e vitamine del gruppo B, non solo riesce a svolgere anche attività stimolante inducendo i follicoli in riposo a produrre un nuovo pelo, a prolungare la fase di crescita dei follicoli già in attività (aumentata vitalità delle cellule epiteliali), ma anche, ad inibire l'enzima coinvolto nella caduta dei capelli senza alterare i valori di testosterone (AGA) .

La sinergia di questi due effetti, fanno pensare all'estratto di Maca come ad un fitocomplesso valido ed efficace nella cura sia dell'alopecia androgenetica che delle calvizie comune.

La combinazione della MACA con opportuni quantità di sostanze bioattive (con differenti target d'azione) presenti in altre matrici vegetali (Serenoa Repens, Ginseng, Bardana,etc.) può rappresentare un importante valore aggiunto.

La sinergia d'azione di questi numerosi estratti, infatti, potrebbe essere più efficace ed il risultato finale super-additivo. se in una miscela complessa di composti bioattivi non tutti agiscono sullo

[17] Gasco M, Villegas L, Yucra S, Rubio J, Gonzales GF (2007) Effect dose–response of red maca on benign prostate hyperplasia in male rats. Phytomedicine 14:460–464.

stesso target biologico, ma su diversi target nello stesso processo patologico (inibizione enzimatica, biodisponibilità, stabilità, ecc) l'effetto finale risulterà potenziato e anche considerevolmente maggiore rispetto ad una loro semplice sommatoria.

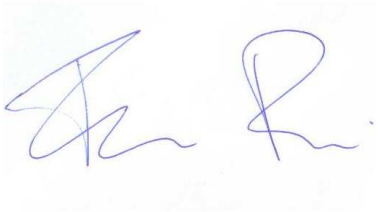
In conclusione possiamo affermare che l'ottimale detersione del cuoio capelluto, ottenuta con prodotti a base di miscele di estratti vegetali, è una valida premessa per intervenire sulle svariate anomalie del capello e per un corretto trofismo del bulbo pilifero.

Infatti, questi prodotti tendono ad attenuare ed eliminare la forfora, la seborrea, la dermatite seborroica, il prurito e tutte le impurità, che provocano ostacoli all'eutrofismo pilare, agevolando il distacco dei vecchi capelli in telogen e favorendo la crescita di quelli in anagen.

La successiva fase nutriente, grazie ai numerosi principi attivi, costituiti da vitamine, aminoacidi, proteine, oligoelementi, fitocomplessi ad attività inibente sulla 5 alfa reduttasi, determina un forte potere stimolante sulla papilla rilevabile con un miglioramento della fase anagen e riduzione della fase telogen, premessa fondamentale per diminuire la caduta e porre basi per favorire una eventuale ricrescita (dove i bulbi la rendono possibile) con un irrobustimento ed inspessimento dei fusti pilari già esistenti.

Rende 20-3-2012

Dott. Francesco Puoci



Test in Uso
Valutazione dell'efficacia cosmetica

Forfora

Seborrea

Rigenerazione Fibra Capillare

Denominazione : Linea Cosmetica MACA REPAIR

Committente:
Luogo : presso SALONI di ACCONCIATURA PROFESSIONALI
Controllo e stesura relazione: Prof. Barbini Nicola Luigi – Docente di Cosmetologia e Metodologie Termali c/o
Università della Calabria
Università di Salerno
Università di Ferrara

SCOPO DEL TEST

Scopo di questo studio è stato quello di:
valutare l'efficacia cosmetica di Maca Repair per problemi tricologici per le seguenti problematiche
Forfora
Seborrea
Rigenerazione Fibra Capillare
L'efficacia cosmetica è stata valutata dopo 45 giorni:
- con metodo di autovalutazione soggettiva dei volontari partecipanti alla sperimentazione che hanno espresso il proprio giudizio in relazione alla scomparsa, totale o parziale, della problematica lamentata.
- con valutazione obiettiva dei professionisti titolari dei saloni
- con controllo della persona responsabile del controllo dati

METODO
Le condizioni sperimentali adottate (area cutanea, modalità di utilizzo del prodotto, frequenza e durata del trattamento) hanno riprodotto le normali condizioni d'uso previste. Il test è stato eseguito su un gruppo di volontari rappresentativo dei potenziali futuri consumatori.
Il rispetto delle condizioni sperimentali da parte dei volontari partecipanti al test è stato valutato con un questionario al termine della sperimentazione.
Il giudizio dei volontari è stato preso in considerazione in quanto potrebbe riflettere quello dei potenziali consumatori.

STRUTTURA DELLO STUDIO
Questo studio è stato eseguito in cieco singolo.

DATE DI ESECUZIONE DEL TEST
Inizio: 01 febbraio 2012
Fine: 15 marzo 2012

NUMERO DI VOLONTARI
Sono stati arruolati complessivamente nr. 6 volontari

VALUTAZIONE
La valutazione è stata adottata tramite giudizi da parte del
CONSUMATORE
PROFESSIONISTA
CONTROLLO
La scala adottata è la seguente
ECCELLENTE
BUONO
DISCRETO
SUFFICIENTE
INSUFFICIENTE
SCARSO
Il giudizio tiene conto del momento **T0** di partenza e del **Tfinale** tramite anamnesi visiva e soggettiva dello stato di partenza e di arrivo .

PROBLEMA, TRATTAMENTO e RISULTATO
Nr 1. Donna
T0 Problema:
Seborrea
Frequenza lavaggio prima del trattamento – 1 per/die
Trattamento:
Lozione Seboregolatrice, Shampoo Seboregolatore e Balsamo Condizionante
Tfinale Risultato:
Netto miglioramento ottenuto dopo già pochi giorni dall'inizio dell'applicazione di shampoo e lozione, si sono verificati lievissimi arrossamenti all'applicazione della lozione nonostante la cliente trovasse gradevole la sensazione anche nelle ore successive.
Pochi giorni dopo l'inizio del trattamento si è resa necessaria l'applicazione ripetuta della lozione sebo anche senza effettuare lo shampoo, uso ovviamente in modiche quantità onde evitare d'appesantire oltre modo i capelli, riuscendo poi ad avere una situazione normalizzata. Si è preferito continuare il trattamento del condizionante solo sulle punte per evitare un eccessivo appesantimento del capello.
Al termine del trattamento la cliente ha ottenuto tempi molto più dilatati tra un lavaggio e l'altro con remissione del fenomeno dell'eccesso di sebo.
Giudizio consumatore : ECCELLENTE
Giudizio professionista : ECCELLENTE
Giudizio controllo : BUONO

Nr. 2 Donna
T0 Problema:
Seborrea
capelli sfibrati tendente alla rottura
Frequenza lavaggio prima del trattamento – 1 per/die
Trattamento:
Lozione Seboregolatrice, Shampo Seboregolatore e Balsamo Condizionante
Tfinale Risultato:
Buono il miglioramento e il risultato sebonormalizzante, non completamente risolto il problema della "secchezza" dei capelli sulle lunghezze e sulle punte. L'uso del condizionante in modalità impacco e sotto fonte caldo/umido è risultato a volte troppo ricco se applicato su radici, lunghezze e punte.
Anche questa cliente ha confermato la sensazione di piacevolezza donata dall'applicazione della lozione. .
Giudizio consumatore : ECCELLENTE
Giudizio professionista : BUONO
Giudizio controllo : BUONO

Nr.3 Donna
T0 Problema:
Forfora
Cute Desquamata
Frequenza lavaggio prima del trattamento – 1 per/die
Trattamento:
Lozione Dermopurificante, Shampoo dermopurificante e Balsamo Condizionante
Tfinale Risultato:
la cliente dopo poche applicazioni di shampoo e lozione ha risolto il problema della desquamazione totalmente,arrivando a poter lavare i capelli ogni 10 giorni senza la ricomparsa di pellicola e desquamazione. Si sono ottenuti migliori risultati applicando la lozione qualche ora prima dello shampo e massaggiandola in modo da consentire un miglior distacco della "pellicola" così poi da effettuare una detersione più profonda.
NOTA si è verificato un leggero inaridimento delle punte, già leggermente sfruttate da colorazione.
Giudizio consumatore : ECCELLENTE
Giudizio professionista : ECCELLENTE
Giudizio controllo : ECCELLENTE

Nr. 4 Donna
T0 Problema:
Forfora
Seborrea
forte desquamazione
Trattamento:
Lozione Dermopurificante, Lozione Seboregolatrice, Shampo dermopurificante e Balsamo Condizionante
Tfinale Risultato:
si sono ottenuti ottimi risultati soprattutto per quanto riguarda l'eliminazione della forfora che era il problema più fastidioso per la cliente. Anche l'effetto sebo normalizzante è stato soddisfacente permettendo di arrivare a tempi molto più lunghi tra un lavaggio e l'altro, sempre però con un cute in condizioni più che discrete. Si è verificato un leggero inaridimento delle lunghezze come nei casi precedenti non totalmente risolvibili con il condizionante.
Giudizio consumatore : ECCELLENTE
Giudizio professionista : BUONO
Giudizio controllo : BUONO

Nr.5 Donna
T0 Problema:
Seborrea
Prurito cutaneo.
Trattamento:
Lozione Seboregolatrice, Lozione Calmante rinfrescante, Shampo Seboregolatore
Tfinale Risultato:
dopo il trattamento la cute si mantiene pulita, i capelli non pesanti ed anche il prurito rimane molto limitato anche a distanza di diversi giorni dal precedente lavaggio con cute rosa e in ottime condizioni.
Giudizio consumatore : ECCELLENTE
Giudizio professionista : BUONO
Giudizio controllo : BUONO

Nr. 6 Donna
T0 Problema:
Seborrea
Desquamazione cutanea
Trattamento:
Lozione Dermopurificante, Lozione Seboregolatrice, Shampo dermopurificante, Balsamo Condizionante.
Tfinale Risultato:
dopo il trattamento la cute è tornata di colore rosa, scomparsa di forfora e netta diminuzione dell'eccesso di sebo. Necessità di lavaggio molto meno frequente .
Giudizio consumatore : ECCELLENTE
Giudizio professionista : BUONO
Giudizio controllo : BUONO

Dr .Barbini Nicola Luigi
consulente industriale

CONCLUSIONI

L'utilizzo di Maca Repair, dopo 45 giorni di trattamento, nell'utilizzo delle appropriate lozioni, shampo e balsamo:

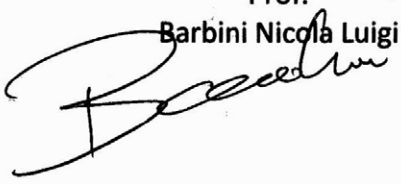
Giudizio di Efficacia cosmetica

1. Ha ridotto sensibilmente la presenza di forfora
2. Ha ridotto sensibilmente la presenza di eccesso di sebo sulla cute e sui capelli permettendo di diminuire i lavaggi per die
3. Ha ristabilito l'equilibrio idrolipidico permettendo l'eliminazione di zone arrossate , con un risultato visibile di cute sana
4. Ha ridotto il fenomeno fastidioso del prurito

Giudizio Sensoriale di utilizzo :

1 . I prodotti sono risultati gradevoli come TEXTURE e PROFUMAZIONE
2 . la detersione è risultata piacevole ed efficace

Prof.
Barbini Nicola Luigi



Via Galeno , 24 – 20126
Milano – Italia

Scheda Tecnica Maca
(Lepidium Meyenii Walp)

MACA SCHEDA PRODOTTO

Nome Botanico: LEPIDIUM MEYENII

:	*Angiosperms-Eudicots*
	Rosids
Ordine:	*Brassicalesc*
Famiglia:	*Brassicacee/Crucifere*
Genere:	*Lepidium*
Specie:	*L. Meyenii*

Origine: PERU' (qualche varietà in Bolivia)

La MACA cresce spontaneamente in Perù, a 3000-4200m di altitudine, resistendo alle condizioni climatiche estreme delle regioni andine dove vive spontaneamente in balia dell'escursione termica: sembra che si serva di un particolare meccanismo di autoprotezione che ha sviluppato in molte migliaia di anni. E' coltivata sin dal 1600 a. C come pianta annuale e biennale ed ha la caratteristica di impoverire fortemente il terreno di coltivazione.

La Maca è l'unico membro del suo genere con un ipocotile carnosa, che si fonde con il fittone per formare una rozzo corpo piriforme rovesciato. La Maca varia notevolmente nelle dimensioni e nella forma della radice, che può essere triangolare, circolare appiattita, sferica o rettangolare, l'ultima delle quali costituisce la radice più grande. Recentemente sono stati riprodotti ceppi specifici di colore per studiare le loro diverse proprietà nutrizionali e terapeutiche. Le radici color crema sono le più ampiamente diffuse e sono caratterizzate dalla loro dolcezza e da una maggiore dimensione. La Maca nera è considerata la più attiva nella promozione dell'energia ed è sia dolce sia leggermente amara nel gusto La Maca rossa sta diventando popolare ed si è dimostrata clinicamente attiva nel ridurre la dimensione della prostata nei topi. Questi tre ecotipi sono i più comunemente coltivate ed esportati.

La parte della pianta impiegata è la radice tuberiforme, che per il suo elevato valore nutritivo ricopre da sempre un ruolo fondamentale nell'alimentazione delle popolazioni indigene e dei loro animali. Le straordinarie virtù nutrizionali e medicamentose della Maca erano note già agli Inca, che lo consideravano un dono degli dei, riservato a guerrieri e sacerdoti. La Maca è stata utilizzata anche come moneta di scambio. Con l'arrivo dei conquistatori spagnoli la Maca fu conosciuta anche in Europa, dove venne apprezzata soprattutto per l'effetto positivo sulla fertilità e per le sue proprietà afrodisiache. A partire dagli anni 1960-'70 la radice della Maca ha cominciato ad essere impiegata in medicina con un razionale scientifico più rigoroso, ed attualmente è apprezzata per la capacità di determinare un generale stato di benessere psico-fisico, che la rende un integratore ideale nella moderna alimentazione, tanto da meritare il nome di **Ginseng peruviano**.

Caratteristiche

La MACA rientra tra le piante adattogene, cioè capaci di aumentare le resistenze dell'organismo. La MACA lavora a livello neuroendocrino presentando una struttura biochimica simile a quella del nostro **PREGNENOLONE,** (→ vedi box a lato), sostanza prodotta all'interno delle nostre cellule mediante le ghiandole surrenali, ma anche dalla pelle, testicoli,

Pregnenolone è un prodotto metabolico naturale del colesterolo estremamente versatile e il precursore di numerose e importanti sostanze (ormoni) messaggere endogene. Tra l'altro Pregnenolone è la sostanza madre degli ormoni sessuali (estrogeno, testosterone), degli ormoni dello stress (cortisone, cortisoli) e di DHEA. Poiché la quantità di Pregnenolone prodotta nel corpo diminuisce con l'avanzare dell'età, si riducono anche le funzioni metaboliche dipendenti dagli ormoni steroidi. La regolare integrazione di Pregnenolone è in grado di riattivare queste funzioni metaboliche, di esercitare un'azione benefica su numerose malattie, e di proteggere il corpo dal declino fisico legato all'età. Per questi motivi Pregnenolone è considerato l'ormone della «sorgente dell'eterna giovinezza» come DHEA.

Il metabolismo di Pregnenolone è molto complesso. Tutti i componenti di questa categoria di sostanze ormonali di base hanno una caratteristica in comune e precisamente la struttura steroide definita chimicamente. Pregnenolone è il primo prodotto metabolico che si forma dopo l'assorbimento del grasso proveniente dall'alimentazione o da sostanze grasse (colesteroli) derivate da questo processo e costituisce l'elemento più importante per la produzione di ormoni steroidi endogeni. Dal momento che Pregnenolone è una sostanza precursore, l'organismo produce sempre la quantità di elementi steroidi di cui ha bisogno al momento. La quantità di Pregnenolone disponibile nel corpo (endogeno) si riduce con l'avanzare dell'età, però non è stato ancora possibile determinare chiaramente che una sua diminuzione sia legata ad una diminuzione del desiderio sessuale.

ovaie e, in grande quantità, dal sistema nervoso.
Prodotto ricco in carboidrati, proteine, aminoacidi e nutrienti essenziali. Il prodotto è considerato utile per incrementare l'energia, il vigore fisico e mentale con effetti antistress ed energizzanti. E' particolarmente indicato per contrastare la fatica cronica e della mente.
Tra le altre attività offerte dalla MACA vi è l'utilizzo nel trattamento dell'impotenza maschile e nel trattamento dei disordini mestruali e nella pre-post-menopausa.

Costituenti fitochimici

- Alcaloidi, Beta-ecdysone, p-metossi-benzil isotio-cianato.
- Vitamine (A,B1,B2, B12,C,D,E) e flavonoidi
- Aminoacidi e acidi grassi essenziali
- Minerali (Calcio, fosforo, ferro, iodio, magnesio, potassio, rame, zinco)
- Steroli (stigmasterolo, sitosterolo, campesterolo, ergosterolo)
- Tannini

Proprietà ed applicazioni Nutriceutiche

- **Attività immunostimolante**.
  La Maca è nota per il suo potere adattogeno: aumenta le resistenze aspecifiche dell'organismo contro lo stress psico-fisico e diverse infezioni patologiche (come ad esempio la tubercolosi), ottimizza il metabolismo energetico cellulare e normalizza le funzioni fisiologiche, ristabilendo l'omeostasi. Prerogativa dell'adattogeno, inoltre, è l'assoluta sicurezza, non presenta cioè effetti tossici o collaterali indesiderati.
- **Attività anti-invecchiamento**.
  L'assunzione della Maca aiuta a ritardare i processi dell'invecchiamento. Grazie all'apporto di vitamine antiossidanti (vit. A, C, E), flavonoidi, acidi grassi essenziali, fosforo ed oligoelementi in genere, la radice della Maca possiede straordinarie virtù energizzanti, contribuendo al mantenimento del vigore fisico, compreso quello sessuale, e della lucidità mentale. Inoltre l'assunzione costante della Maca previene l'incanutimento e la caduta dei capelli, stimolandone la crescita, incrementa il grado di idratazione della pelle e la tonicità dei tessuti.
- **Attività anabolizzante**.
  Per il suo contenuto in steroli quali il b-ecdisone, la Maca costituisce un'alternativa naturale e sicura agli anabolizzanti. Body builders, atleti e sportivi confermano che la sua assunzione non solo incrementa la forza e la resistenza fisica, ma contribuisce anche allo sviluppo della massa muscolare.
- **Incremento della densità ossea**.
  La radice della Maca apporta alti livelli di calcio e sali minerali in genere in forma facilmente assorbibile. La sua assunzione, quindi, è consigliabile quando il fabbisogno di questi elementi aumenta, ad esempio durante la crescita, la gravidanza e l'allattamento, la menopausa; si è inoltre rivelato utile per accelerare la guarigione delle fratture e nel trattamento delle patologie legate al decremento della densità ossea, quali decalcificazione e osteoporosi
- **Coadiuvante nel trattamento delle anemie**.
  L'elevato contenuto di ferro e vitamina B12 stimola la produzione dei globuli rossi, rendendo la Maca un valido coadiuvante nel trattamento delle anemie di modesta e media entità.

- **Regolazione dell'asse ipotalamo-ipofisario**.
  L'attività adattogena della Maca si esplica in modo particolare a livello della regolazione dell'attività endocrina, specie quella sotto il controllo dell'asse ipotalamo-ipofisario. Per questo motivo la Maca trova impiego nel trattamento di molte disfunzioni ormonali legate alla sfera sessuale, e riguardanti la fisiologia sia maschile che femminile.
- **Attività afrodisiache e trattamento dell'impotenza**.
  Studi clinici condotti da numerosi medici americani dimostrano che l'assunzione della Maca ha effetti positivi sulla vita sessuale di entrambi i sessi, incrementando la libido e migliorando le prestazioni sessuali. Inoltre si è rivelato estremamente efficace nel trattamento delle disfunzioni erettili e dell'impotenza maschile, sia che si manifesti come stato patologico, sia che insorga fisiologicamente con l'avanzare dell'età.
- **Trattamento della sterilità maschile e femminile.** .
  Da secoli la Maca è impiegata per aumentare le capacità riproduttive di uomini e animali. Oggi esistono numerosi studi a riguardo: quattro alcaloidi isolati dalla radice della Maca, somministrati a ratti di entrambi i sessi, hanno dimostrato di incrementare l'oogenesi nelle femmine e la spermatogenesi nei maschi, e gli stessi risultati sono stati raggiunti con l'assunzione della radice essiccata. Gli effetti su ovaie e testicoli compaiono già dopo 72 ore dalla somministrazione, e non sono dovuti ad ormoni vegetali, ma all'azione dei suddetti alcaloidi sull'asse ipotalamo-ipofisario, che nella specie umana si ripercuote anche sui reni, sul pancreas e sulla tiroide.
- **Disfunzionalità ovarica, menopausa.** .
  I ginecologi americani prescrivono la Maca per regolare la funzionalità ovarica. In menopausa è preferito alla terapia ormonale sostitutiva, perché, al contrario degli ormoni esogeni, stimola naturalmente le ovaie e le altre ghiandole endocrine a produrre gli ormoni di cui l'organismo ha bisogno. E' dimostrato che l'assunzione della Maca allevia in maniera significativa i sintomi tipici che precedono e accompagnano la menopausa (vampate di calore, depressione e stanchezza, tachicardia, costipazione, perdita di tessuto osseo, secchezza vaginale). In caso di menopausa precoce l'uso della Maca può consentire la ripresa di un ciclo mestruale regolare, mentre in seguito ad isterectomia, con o senza rimozione delle ovaie, fa registrare in breve tempo un incremento dei livelli ematici di estradiolo e un miglioramento delle condizioni generali: .
  In base agli studi clinici si consiglia l'assunzione della Maca prima della menopausa, per mantenere le ovaie in buono stato ed ottenere in seguito maggiori benefici.
- **Proprietà toniche e rinforzanti la memoria**

Nota: diverse di queste proprietà sono riportate in letteratura e, spesso, fanno parte della tradizione locale. Alcuni degli studi effettuati non hanno il gruppo di controllo e non sono stati effettuati verso placebo, pertanto il loro significato deve essere considerato relativo.

Indicazioni ·

Può essere impiegata dagli sportivi, (ottima per chi compie sforzi fisici in montagna), contribuisce allo sviluppo della massa muscolare. Studenti e manager possono trarne giovamento per superare momenti di stress psico-fisico. La Maca, inoltre, rallenta i processi degenerativi dell'invecchiamento, previene la caduta dei capelli e mantiene il grado di idratazione della pelle e della tonicità dei tessuti.
In particolare gli impieghi possono essere:

- Stress psico-fisico (stati depressivi, alimentazione di sportivi, studenti, anziani, ecc.)
- Fratture, decremento delle densità ossea
- Coadiuvante nel trattamento di alcuni tipi di tumore
- Coadiuvante nella cura dell'anemia
- Trattamento dell'impotenza maschile
- Trattamento delle disfunzioni ovariche, compresa la menopausa
- Trattamento della sterilità maschile e femminile
- Miglioramento dei problemi di attenzione e concentrazione dei bambini.

Dosaggi di impiego e tossicità

La dose di Maca da assumere giornalmente non è ancora stata standardizzata in modo rigoroso, e può variare in funzione delle esigenze personali. In media si consigliano da 5 a 20g di radice essiccata al giorno oppure 400 - 1000 mg di estratto secco.
Benché non siano stati riscontrati effetti tossici veri e propri, esiste sempre la possibilità di rare reazioni allergiche in individui ipersensibili. L'uso della Maca, inoltre, richiede un'accurata valutazione medica in soggetti maschi con elevati livelli di PSA (antigene prostatico specifico) o con precedenti di cancro alla prostata, e in donne che abbiano avuto o siano a rischio di cancro al seno. E' invece sconsigliato, a causa dell'elevato contenuto di iodio, in caso di ipertiroidismo. Il suo impiego deve avvenire sotto stretto controllo medico anche durante la gravidanza e l'allattamento.

Forme di impiego

La radice della Maca rientra da secoli nell'alimentazione delle popolazioni andine, che lo consumano fresco, in pietanze e bevande tipiche, o essiccato. La radice secca può essere conservata molto a lungo, mantenendo pressocché inalterate le sue caratteristiche nutrizionali; la polvere può essere reidratata (sciolta in acqua, in succhi di frutta, o mescolata ai cibi) o consumata in diverse forme: tavolette, capsule, compresse, ecc. Se si desidera utilizzarne l'estratto, un'infusione a freddo è ideale per non degradare le saponine presenti.

In Perù, la Maca è preparata e consumata in vari modi, anche se tradizionalmente è sempre cotta. L'ipocotile appena prelevato può essere arrostito in una buca (chiamato huatia), e questa è considerata una prelibatezza. Le radici fresche sono di solito disponibili solo in prossimità delle coltivazioni. La radice può anche essere schiacciata e lessata per la produzione di un liquido dolce e denso, essiccata e mescolata con il latte per formare una polenta o con altre verdure o cereali per produrre una farina che può essere utilizzata in cottura. Se fermentata, può essere prodotta una birra debole chiamata "chicha de maca". Le foglie possono anche essere preparate in insalata o cotte.

La crescente domanda del settore degli integratori è stato uno dei motivi principali per l'espansione della Maca. Il prodotto di rilievo è farina di MACA, che si ottiene dalle dure radici essiccate. In Perù, la farina di MACA è usata in cottura come una base e un aroma. L'industria degli integratori utilizza sia le radici secche sia la farina di MACA per diversi tipi di trasformazione e di estratti concentrati. Un'altra forma comune è la Maca che ha subito la gelatinizzazione. Si tratta di un processo di estrusione, a volte utilizzato per altre verdure, che rimuove la fibra dalle radici con leggero calore e pressione. La MACA è una delle radici in cui la gelatinizzazione rende il prodotto più efficiente per la digestione. La Maca gelatinizzata è molte volte più forte della polvere ottenuta dalla radice, ed è impiegata principalmente per uso terapeutico, medicinali e integratori.

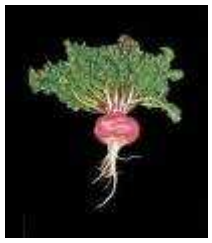
Matrice operativa

AREA UMANA	SVILUPPO
Nutrizionale/Alimentare	Fiocchi, Snacks, Biscotti, Marmellate, Prodotto finito in capsule, Polvere
Bevande	Energetiche (tipo Red Bull od altre)
Integratori/produzioni alimentari	Yogurt, Latte, Pasta, Succhi di frutta

AREA DERMOCOSMETICA	SVILUPPO
Prodotti bellezza corpo	Creme, Lozioni

AREA ANIMALI	SVILUPPO
Integrato in mangimi per animali	Per animali di allevamento e piccoli animali

Altre immagini



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Profilo nutrizionale di radice secca di MACA

Tra i costituenti fitochimici:
Alcaloidi, Beta-ecdysone, p-methoxybenzyl isothiocynate
Vitamine (A, B1, B2, B12, C, D, E) e flavonoidi
Aminoacidi ed acidi grassi essenziali
Steroli (Stigmasterolo, Sitosterolo, Campesterolo, Ergosterolo)
Tannini

	100 g
Componenti	Proteine 10-14 g Carboidrati 60-75 g Grassi (lipidi) 0,6-2,2 g Fibre 6,0-8,5 g Frassino 4,9 g Steroli 50-100 mg Calories 325
Vitamine	B2 390 mcg B6 1.140 mcg C 286 mg Niacina 5.650 mcg
Amminoacidi	Alanina 631 mg Arginina 994 mg Acido aspartico 917 mg Acido glutaminico 1565 mg Glicina 683 mg Istidina 419 mg HO-Prolina 260 mg Isoleucina 474 mg Leucina 910 mg Lisina 545 mg Metionina 280 mg Fenilalanina 553 mg Prolina 5 mg Sarcosina 7 mg Serina 504 mg Treonina 331 mg Triptofano 49 mg Tirosina 306 mg Valina 793 mg
Minerali	Calcio 250 mg Rame 6 mg Ferro 15 mg Iodio 520 mcg Manganese 800 mcg Potassio 2.050 mg Sodio 19 mg Zinco 3800 mcg
Grassi/lipidi	Linoleico 720 mcg Palmitico 520 mcg Oleico 245 mcg

Principali Studi Scientifici

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Mini-Review

Molecular mechanisms of androgenetic alopecia

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Abstract

Androgenetic alopecia (AGA) is hereditary and androgen-dependent, progressive thinning of the scalp hair that follows a defined pattern. While the genetic involvement is pronounced but poorly understood, major advances have been achieved in understanding principal elements of the androgen metabolism involved: androgen-dependent processes are predominantly due to the binding of dihydrotestosterone (DHT) to the androgen receptor (AR). DHT-dependent cell functions depend on the availability of weak androgens, their conversion to more potent androgens via the action of 5alpha-reductase, low enzymatic activity of androgen inactivating enzymes, and functionally active AR present in high numbers. The predisposed scalp exhibits high levels of DHT, and increased expression of the AR. Conversion of testosterone to DHT within the dermal papilla plays a central role, while androgen-regulated factors deriving from dermal papilla cells are believed to influence growth of other components of the hair follicle. Current available treatment modalities with proven efficacy are oral finasteride, a competitive inhibitor of type 2 5α-reductase, and topical minoxidil, an adenosine-triphosphate-sensitive potassium channel opener which has been reported to stimulate the production of vascular endothelial growth factor in cultured dermal papilla cells. Since the clinical success rate of treatment of AGA with modulators of androgen metabolism or hair growth promoters is limited, sustained microscopic follicular inflammation with connective tissue remodeling, eventually resulting in permanent hair loss, is considered a possible cofactor in the complex etiology of AGA.

Keywords: Androgenetic alopecia; Androgen metabolism; Androgen receptor; Polygenic inheritance; Follicular microinflammation; Permanent hair loss

Androgenetic alopecia (AGA), also referred to as male-pattern hair loss or common baldness in men, and as female-pattern hair loss in women, affects at least 50% of men by the age of 50 years, and up to 70% of all males in later life (Norwood, 1975). Estimates of its prevalence in women have varied widely, though recent studies claim that six percent of women aged under 50 years are affected, increasing to a proportion of 30–40% of women aged 70 years and over (Norwood, 2001). The hair loss is heritable, androgen-dependent, and occurs in a defined pattern. It is assumed that the genetically predisposed hair follicles are the target for androgen-stimulated hair follicle miniaturization, leading to gradual replacement of large, pigmented hairs (terminal hairs) by barely visible, depigmented hairs (vellus hairs) in affected areas (Paus and Cotsarelis, 1999). The result is a progressive decline in visible scalp hair density. While male pattern AGA is characterized by its typical bitemporal recession of hair and balding vertex, female pattern AGA is set apart by its diffuse thinning of the crown and intact frontal hairline. While prerequisites are thus a genetic predisposition

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and androgens, clinical practice has shown us that simply blocking androgens does not result in the conversion of miniaturized follicles to terminal ones in advanced alopecia. On histologic examination of scalp biopsies, the miniaturization of terminal hairs is frequently associated with perifollicular lymphocytic infiltration, and eventually fibrosis (Jaworsky et al., 1992; Whiting, 1993). Therefore it is conceivable that the role of this microscopic follicular inflammation causing fibrosis below the shortened balding follicle has been underestimated, though it seems likely that this would prevent the follicle to reform a terminal hair follicle.

It is the aim of this paper to review the molecular mechanisms resulting in AGA, as far as androgens, genetics, and inflammatory phenomena are involved.

1. Hair-follicle cycling and signaling molecules controlling hair growth

The hair-growth cycle: The hair follicle is subject to constant turnover in the course of perpetual cycles through various stages of proliferation (*anagen*), involution (*catagen*), and resting (*telogen*), with regeneration in the successive hair cycle (Fig. 1). It is a major characteristic of anagen that not only the hair shaft is growing but that most epithelial hair follicle compartments undergo proliferation, with the hair matrix keratinocytes located around the dermal papilla showing the highest proliferative activity. Also, the newly formed hair shaft is pigmented by the follicle pigmentary unit (Paus and Cotsarelis, 1999). During the following catagen stage of the hair cycle, hair follicles enter a highly controlled process of involution that is characterized by a burst of programmed cell death (apoptosis) in the majority of follicular keratinocytes, termination of pigment production, substantial extracellular matrix-remodeling, and condensation of the dermal papilla (Paus and Cotsarelis, 1999). The resulting shortening of the regressing epithelial strand is associated with an upward movement of the dermal papilla within the connective tissue sheath of the follicle. In telogen the hair shaft matures into a club hair, which is held tightly in the bulbous base of the follicular epithelium, before it is eventually shed from the follicle, usually as a result of combing or washing. It is still unresolved whether shedding of the telogen hair (*teloptosis*) is also an active, regulated process or represents a passive event that occurs at the onset of subsequent anagen, as the new hair grows in (Paus and Cotsarelis, 1999; Pierard-Franchimont and Pierard, 2001). There are considerable variations in length of these stages depending on the body site location, with the duration of anagen determining the type of hair produced, particularly its length (Paus and Cotsarelis, 1999). On the scalp, hairs remain in anagen for a 2–7-year period of time, whereas that of telogen is 100 days, leading to a ratio of anagen to telogen hairs of approximately 9:1. On average the amount of new scalp hair formation essentially matches the amount that is lost due to shedding (approximately 100/day), thereby maintaining a consistent covering.

Hair growth control: The controls that underlie the hair cycle reside within the hair follicle itself, and are believed to result from changes in the intra- and perifollicular expression of specific regulatory molecules and their receptors (Paus et al., 1999). Much circumstantial evidence suggests that the dermal papilla which is composed of specialized fibroblasts located at the base of the follicle, determines hair follicle growth characteristics, especially the regulation of cell proliferation and differentiation of hair follicle matrix: without papilla fibroblasts and an intimate contact with hair matrix keratinocytes anagen cannot be sustained. Also, hair follicle morphogenesis can be induced by implanting dermal papilla cells under an appropriately receptive epithelium (Jahoda et al., 1984). Finally, it has been shown that implanting few cells of follicle dermal-sheath tissue from the scalp from an adult human male is sufficient to form new dermal papillae and induce new hair follicles in the skin of a genetically unrelated female (Reynolds et al., 1999). There is substantial evidence from bioassays that cultured dermal papilla cells can secrete a number of cytokines, growth factors and other, yet unidentified bioactive molecules that influence growth in other dermal papilla cells, outer root sheath cells, keratinocytes, and endothelial cells (Stenn et al., 1996). Finally, the hair cycle is subjected to cycle modulation by numerous extrinsic influences, such as androgens (Paus, 1996).

Pathobiology of AGA: AGA is characterized by progressive shortening of the duration of anagen with successive hair cycles, leading to decreased numbers

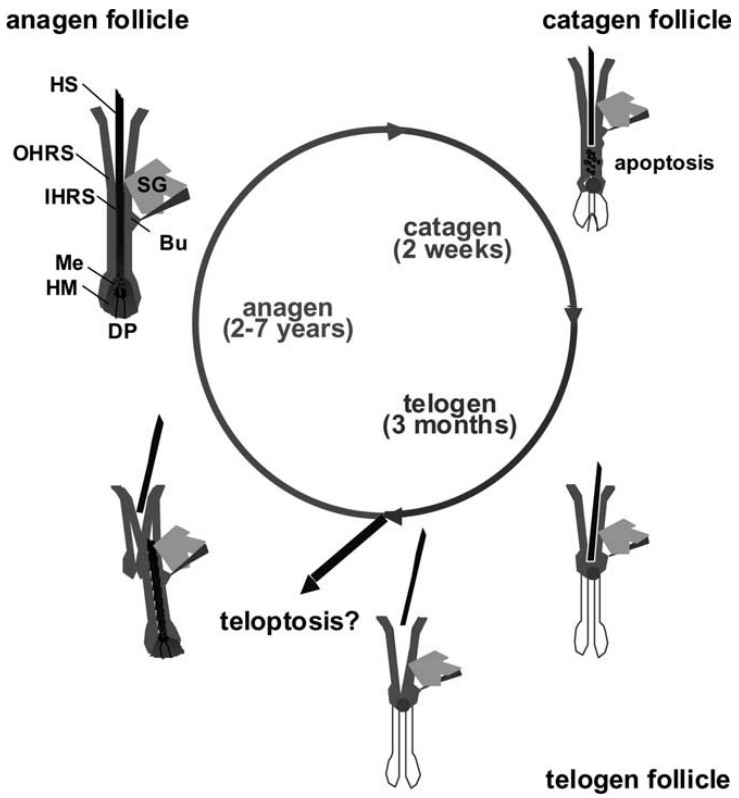


Fig. 1. The hair-growth cycle. Abbreviations: HS = hair shaft; OHRS = outer hair root sheath; IHRS = inner hair root sheath; SG = sebaceous gland; Bu = bulge; Me = Melanocytes; HM = hair matrix; DP = dermal papilla.

of hair in anagen at any given time, and progressive follicular miniaturization with conversion of terminal to vellus-like follicles (Paus and Cotsarelis, 1999). The result is increased shedding of short-lived telogen hairs (telogen effluvium), while the affected hair follicles produce shorter, finer hairs that cover the scalp poorly. Since AGA involves a process of premature termination of anagen associated with premature entry into catagen, it is critically important to dissect the molecular controls of the anagen–catagen transformation of the hair cycle (Paus, 1996). Catagen has been suggested to occur as a consequence of decreased expression of anagen maintaining factors, such as insulin-like growth factor 1 (IGF-1), basic fibroblast growth factor (bFGF), and vascular endothelial growth factor (VEGF), and increased expression of cytokines promoting apoptosis, such as transforming growth factor beta 1 (TGFβ 1), interleukin-1alpha (IL-1α), and tumor necrosis factor alpha (TNFα).

Responses to androgens are obviously also intrinsic to the individual hair follicle: not only does the response vary from stimulation to inhibition of hair growth depending on the body site, but androgen sensitivity also varies within individual areas, i.e. regression in AGA occurs in a patterned, progressive manner. Since many extrinsic hair growth-modulatory factors, such as androgens (Randall et al., 1992), apparently operate at least in part via the dermal papilla, research is currently also focused on identifying androgen-regulated factors deriving from dermal papilla cells.

Of the several factors that have been suggested to play a role in hair growth, so far only insulin-like growth factor (IGF-1) has been reported as altered in vitro by androgens (Itami et al., 1995), and stem cell factor (SCF) has been found to be produced in higher amounts by androgen-dependent beard cells than in control non-balding scalp cells, presumably also in response to androgens (Hibberts et al., 1996). Since SCF is the ligand for the cell surface receptor c-kit on melanocytes, this may also play a role for hair pigmentation.

2. Androgens, androgen metabolism, and the androgen receptor

Androgens: Of various hormones that affect hair growth, the most studied are the androgens, particularly as they pertain to AGA. Since Aristotle first noted that 'maleness' and sexual maturity were required for balding, it was not until 1942 that Hamilton's observations on men deprived of testicular androgens by castration established beyond doubt that androgens, in the form of testosterone or its metabolites, were prerequisites for development of common baldness. Hamilton observed that men who were castrated before puberty did not develop AGA, and that AGA can be triggered in castrated men by injecting testosterone (Kaufman, 1996).

Androgen metabolism: Androgen metabolism comprises glandular and extraglandular production, transport, target cell metabolism, and cellular response. While androgen biology in the adrenals and gonads, and the influence of the pituitary axis go beyond the scope of this review, androgen metabolism within the skin, as it pertains to hair growth and its disorders, is the focus (Kaufman, 1996). The androgen metabolism pathway begins with pregnenolone, a 21 carbon steroid substrate, converted from cholesterol. Following α-hydroxylation at the C-17 position, the action of the enzyme C_{17-20} lyase cleaves distal carbon moieties, leaving a C19 carbon steroid with a C-17 ketone in the distal ring. These '17-ketosteroids' make up a group of weak androgens, such as dehydroepiandrosterone (DHEA), defined by a low affinity for the androgen receptor. These weak androgens, however, can be enzymatically converted to more potent androgens with greater affinity for the androgen receptor, such as testosterone. Testosterone is the major circulating androgen. In women, systemic levels of testosterone are low compared with men, but the more abundant weak androgens serve as a source of precursors for potent androgens, which provide the physiologic or pathophysiologic androgen activity. Only a small fraction of androgens exists as free steroids in the circulation, with an equilibrium between free hormones and protein-bound androgens. The most important protein for androgen binding is sex-hormone binding globulin (SHBG). Normally 70% of testosterone is bound to SHBG, and 19% to albumin. The remainder is circulating unbound. In most target organs testosterone can be metabolized to DHT by the enzyme steroid 5α-reductase. Based on its affinity for the androgen receptor, DHT is fivefold more potent than testosterone. DHT is implicated in the pathogenesis of several disorders, including benign prostatic hyperplasia, prostate cancer, hirsutism, acne vulgaris, and AGA.

Androgen metabolism within skin: The skin and pilosebaceous unit are enzymatically equipped for local metabolism and conversion of sex steroids (Kaufman, 1996). The skin is capable of synthesizing active androgens from the systemic precursor DHEA-sulfate (DHEA-S). The first step is the desulfatation of DHEA-S by the enzyme steroid sulfate (STS). The principal pathways involved in conversion of weak androgens like DHEA to more potent androgens are through activity of the enzymes 3β-hydroxysteroid dehydrogenase-$\Delta^{5\rightarrow4}$-isomerase (3β-HSD), 17β-hydroxysteroid dehydrogenase (17β-HSD), and 5α-reductase. Once formed, potent androgens, such as testosterone and DHT, can be removed by conversion back to the weaker 17-ketosteroids, or are metabolized via other enzymatic pathways, including aromatase, which converts androgens to estrogens, and 3α-hydroxysteroid dehydrogenase to form androsterone and androstanediol. The latter can be glucuronidated to form androgen conjugates that are more rapidly cleared from the circulation. Remarkably, some target tissues, such as the hair follicle, show enhanced androgen metabolism and androgen sensitivity. The activity of enzymes involved in androgen metabolism within the skin has been studied in a variety of tissue preparations. The sebaceous glands in balding skin have been shown to express increased 3β-HSD activity when compared to non-balding scalp areas (Sawaya et al., 1988). Earlier it was shown that plucked human hair follicles or hair follicles from balding stumptailed macaques express considerable 17β-HSD activity (Takashima et al., 1970). In a study of plucked hair follicles from young adults not yet expressing AGA but with a strong family history of baldness, two populations were found, one with high 17β-HSD activity and one with low enzyme activity (Hodgins et al., 1985). The study suggested that low enzyme activity may be related to lesser degrees of balding. More recently, both men and women with AGA were shown to have higher levels of 5α-reductase enzyme activity in frontal

follicles than in their own occipital follicles, whereas higher levels of aromatase were found in their occipital follicles (Sawaya and Price, 1997).

Steroidogenic enzyme mutations: Since STS converts DHEA-S to DHEA that is eventually metabolized to more potent androgens in the periphery, and elevated plasma levels of DHEA-S and DHEA have been reported to correlate with balding in young men, the hypothesis was advanced, that men with genetic STS deficiency (X-linked recessive ichthyosis, XRI) do not or only develop minor forms of AGA. A survey of patients with XRI showed that this was not the case, since these men also showed advanced AGA (Trüeb and Meyer, 2000). In genetically determined deficiencies of the enzymes 3β-HSD, or 17β-HSD, respectively, the presence or absence of AGA has not been investigated so far (Hoffmann and Happle, 2000).

The description of an unusual form of incomplete male pseudohermaphroditism, due to a genetic deficiency of the type 2 steroid 5α-reductase by Imperato-McGinley et al. (1974), implicated DHT as principal mediator of androgen-dependent hair loss. Affected men, who are homozygous for mutation of the gene, do not develop AGA.

Mutations of the human gene encoding aromatase (CYP19) are rare and result in aromatase deficiency. Affected girls show pseudohermaphroditism at birth, and at puberty develop virilization and hirsutism due to an androgen excess, pubertal failure with no signs of estrogen action, hypergonadotropic hypogonadism, polycystic ovaries, and a tall stature. Males are rather tall with eunuchoid skeletal proportions. In theory, females and males might develop early onset of AGA (Hoffmann and Happle, 2000). Consistent with the role of aromatase in avoiding androgen-mediated effects on androgen-dependent hair follicles, is the observation that women taking aromatase inhibitors for the treatment of breast cancer often experience an AGA-like hair loss.

Androgen receptor (AR): Finally, the absence of balding in individuals with the androgen-insensitivity syndrome who lack functional AR clearly demonstrates the need for AR for AGA to occur (Quigley, 1998). All steroid hormones act by diffusing through the plasma membrane into the target cell and binding to specific intracellular receptors. The hormone-receptor complex undergoes conformational changes, exposing DNA-binding sites, and then bind to specific hormone response elements in the DNA, promoting the expression of specific hormone-regulated genes. The AR is believed to be responsible for determining the sensitivity of cells to androgens. Besides androgen insensitivity, various mutations have been described in the gene encoding the AR in a variety of diseases, including spinal and bulbar muscular atrophy (Kennedy's disease), and prostate cancer (Gottlieb et al., 1998). Some of these are associated with functional changes in AR expression. Expression of the AR has also been found to be increased in balding scalp (Randall et al., 1992; Sawaya and Price, 1997). Most recently, polymorphism of the AR gene has been found to be associated with male pattern baldness (Ellis et al., 2001).

3. Genetic involvement

The genetic involvement is pronounced, and the importance of genes concurs with marked racial differences in prevalence of AGA; non-Caucasians often exhibit significantly less balding. While major progress has been done in the understanding of androgen metabolism, the genetic predisposition to AGA remains poorly understood. A very high frequency of AGA has complicated attempts to establish a mode of inheritance. Moreover, it is not clear whether AGA is genetically homogeneous; some authorities suggest that female pattern hair loss is not the female counterpart of male AGA, and not androgen-dependent (Orme et al., 1999). The genes for type 1 and type 2 5α-reductase have been shown not to be associated with the inheritance of AGA (Ellis et al., 1998). Polymorphism of the AR gene is associated with male pattern baldness (Ellis et al., 2001), however, the AR gene is located on the X chromosome and does not explain the relatively strong concordance of the degree of baldness in fathers and sons. No specific gene has been identified so far, though single gene mutations, such as abnormality of the AR, might be necessary, but not sufficient for the phenotype (Ellis et al., 2001). We probably deal with a polygenic inheritance, dependent on a combination of mutations, e.g. in or around the AR gene affecting the expression of the AR, and

other genes controlling androgen levels. Interactions between such genes might account for the tissue-specific and developmental stage-specific expression of the AR that is necessary to explain the characteristic anatomic and temporal patterns of AGA. Other genes relevant to androgens, including those on the Y chromosome might also be examined (Ellis et al., 2001).

4. Hair follicle microinflammation

The limited success rate of treatment of AGA with hair growth promoters or modulators of androgen metabolism means that further pathogenic pathways may be taken into account. The implication of microscopic follicular inflammation in the pathogenesis of AGA has recently emerged from several independent studies (Jaworsky et al., 1992; Mahé et al., 2000; Whiting, 1993). An early study referred to an inflammatory infiltrate of activated T cells and macrophages in the upper third of the hair follicles, associated with an enlargement of the follicular dermal-sheath composed of collagen bundles (perifollicular fibrosis), in regions of actively progressing alopecia (Jaworsky et al., 1992). Horizontal section studies of scalp biopsies indicated that the perifollicular fibrosis is generally mild, consisting of loose, concentric layers of collagen that must be distinguished from cicatricial alopecia (Whiting, 1993). The term 'microinflammation' has been proposed, because the process involves a slow, subtle, and indolent course, in contrast to the inflammatory and destructive process in the classical inflammatory scarring alopecias (Mahé et al., 2000). The significance of these findings has remained controversial. However, morphometric studies in patients with male pattern AGA treated with minoxidil showed that 55% of those with microinflammation had regrowth in response to treatment, in comparison to 77% in those patients without inflammation and fibrosis (Whiting, 1993).

Inflammatory phenomena: An important question is how the inflammatory reaction pattern is generated around the individual hair follicle. Inflammation is regarded as a multistep process which may start from a primary event. The observation of a perifollicular infiltrate in the upper follicle near the infundibulum suggests that the primary causal event for the triggering of inflammation might occur near the infundibulum (Mahé et al., 2000). On the basis of this localization and the microbial colonization of the follicular infundibulum with *Propionibacterium* sp., *Staphylococcus* sp., *Malassezia* sp., or other members of the transient flora, one could speculate that microbial toxins or antigens could be involved in the generation of the inflammatory response. The production of porphyrins by *Propionibacterium* sp. in the pilosebaceous duct has also been considered to be a possible cofactor of this initial pro-inflammatory stress (Mahé et al., 2000). Alternatively, keratinocytes themselves may respond to chemical stress from irritants, pollutants, and UV irradiation, by producing radical oxygen species and nitric oxide, and by releasing intracellularly stored IL-1α. This pro-inflammatory cytokine by itself has been shown to inhibit the growth of isolated hair follicles in culture (Philpott et al., 1996). Moreover, adjacent keratinocytes, which express receptors for IL-1, start to engage the transcription of IL-1 responsive genes: mRNA coding for IL-1β, TNFα, and IL-1α, and for specific chemokine genes, such as IL-8, and monocyte chemoattractant protein-1 (MCP-1) and MCP-3, themselves mediators for the recruitment of neutrophils and macrophages, have been shown to be upregulated in the epithelial compartment of the human hair follicle (Mahé et al., 2000). Besides, adjacent fibroblasts are also fully equipped to respond to such a pro-inflammatory signal. The upregulation of adhesion molecules for blood-borne cells in the capillary endothelia, together with the chemokine gradient, drive the transendothelial migration of inflammatory cells, which include neutrophils through the action of IL-8, T cells and Langerhans cells at least in part through the action of MCP-1. After processing of localized antigen, Langerhans cells, or alternatively keratinocytes, which may also have antigen presenting capabilities, could then present antigen to newly infiltrating T lymphocytes and induce T-cell proliferation. The antigens are selectively destroyed by infiltrating macrophages, or natural killer cells.

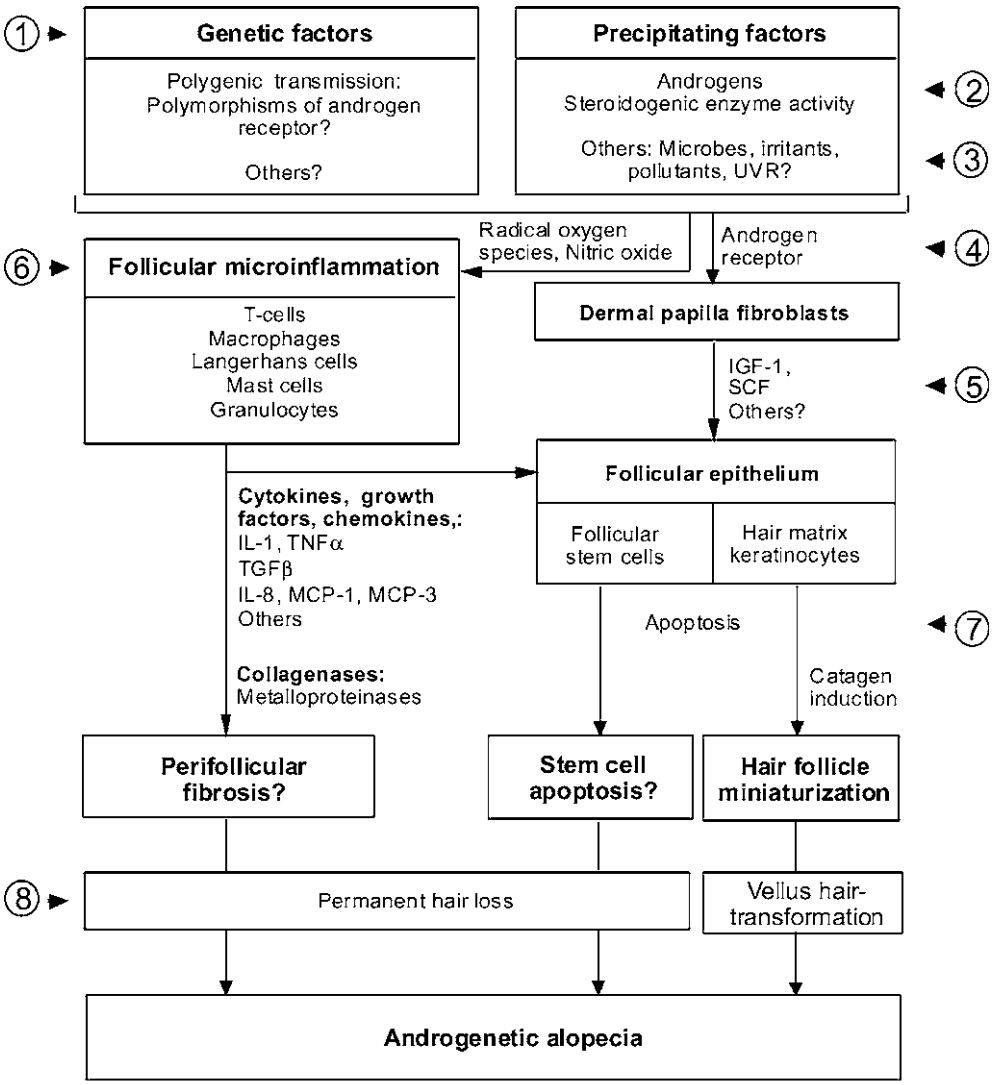
Perifollicular fibrosis: On the occasion that the causal agents persist, sustained inflammation is the result, together with connective tissue remodeling, where collagenases, such as matrix metalloproteinase (also transcriptionally driven by pro-inflammatory cytokines) play an active role (Mahé et al., 2000). Collagenases are suspected to contribute to the tissue changes in perifollicular fibrosis.

Permanent alopecia: Generally, permanent alopecia is the result of irreversible damage to the putative site of follicular stem cells in the 'bulge' area of the outer-root sheath in the superficial portion of the hair follicle (Lavker et al., 1993). In most of inflammatory scarring alopecias, e.g. *lichen planopilaris*, *lupus erythematosus*, and *pseudopelade (Brocq)*, the inflammation involves this area. In the recently described *fibrosing alopecia in a pattern distribution* (Zinkernagel and Trüeb, 2000), patients with AGA have additional clinical and histological features of inflammation and fibrosis limited to the area of androgenetic hair loss. A *lichen planopilaris*-type inflammation involving the bulge area presumably irreparably damages follicle stem cells. The preference of this site of the follicle for the immunologic attack may be related to the fact, that in contrast to the proximal hair follicle, the isthmus and infundibulum area do not bear any immune privilege (Paus, 1997).

5. Concluding remarks

Clinical and investigative advances have helped us to understand some of the pathogenic steps leading to androgenetic hair loss (Fig. 2). Besides androgens and genetic imbalance, additional pathogenic factors are suspected, such as microbial flora, endogenous and exogenous stress, microinflammation, and possibly others. While further suspects are likely to be exposed, individual diversity of causal agents, as well as of the sequence of events, or combined factors, must be kept in mind, when addressing the biological conditions contributing to AGA. The large number of therapeutic molecules currently claimed to be active and patented in this field and their limited efficacy in offering a definitive cure of AGA, confirm that the mechanism of AGA is highly complex.

Therapeutic challenges: The aim of therapy is to increase hair coverage of the scalp and to retard progression of hair thinning. Currently, two FDA approved drugs are available for this purpose, oral finasteride, at a dose of 1 mg per day, and topical solution of minoxidil (Price, 1999). Finasteride is a competitive inhibitor of type 2 5α-reductase and inhibits the conversion of testosterone to DHT. The rationale for the use of finasteride to treat AGA in men is based on the absence of AGA in men with congenital deficiency of type 2 5α-reductase, and the presence of increased 5α-reductase activity and DHT levels in balding scalp (Kaufman et al., 1998). Finasteride is contraindicated in women who are or may become pregnant, because 5α-reductase inhibitors may cause malformation of the external genitalia of male fetuses. Minoxidil promotes hair growth through increasing the duration of anagen. It causes hair follicles at rest to grow, and enlarges suboptimal follicles. While minoxidil was developed for treatment of hypertension, and this feature of the drug's action is best understood, its mechanism of action on hair growth is poorly understood. Minoxidil is a potassium-channel opener and vasodilatator, and has been reported to stimulate the production of VEGF in cultured dermal papilla cells (Lachgar et al., 1998). There is evidence that this effect is mediated by adenosine and sulfonylurea receptors, which are well-known target receptors for adenosine-triphosphate-sensitive potassium channel openers (Li et al., 2001). Topical solutions of 2 and 5 percent minoxidil are available for treatment of AGA in men and women. Unfortunately, the efficacy of minoxidil is variable and temporary, making it difficult to predict the success of treatment on an individual basis. Estrogens and antiandrogens are used in women with AGA, although no controlled studies have been done. When a combination of estrogen and a progestin is prescribed for oral contraception or hormonal replacement therapy in women with AGA, care should be taken to select a progestin with no androgenic, or preferably with antiandrogenic activity, e.g. cyproterone acetate. Women with this condition should also avoid androgens and their precursors, such as DHEA, since these may exacerbate hair loss (Price, 1999). So far, the inflammatory component has not been included in treatment protocols for AGA. Finally, it



Therapeutic strategies:

1. Gene therapy? (currently not available)
2. Modifiers of androgen metabolism: finasteride (available for men)
3. Antimicrobial shampoos?
4. Antiandrogens: cyproterone acetate (available for women)
5. Hair growth promoters: minoxidil (available for men and for women)
6. Antiinflammatory agents?
7. Apoptosis modulating agents? (currently not available)
8. Hair transplantation (available), implantation of dermal papilla cells or cells of follicle dermal-sheath (impending)

Fig. 2. Androgenetic alopecia: pathogenic mechanisms and therapeutic strategies.

has been proposed that gene therapy may offer yet another approach on condition that the genes responsible for alopecia are identified (Paus and Cotsarelis, 1999). Given the accessibility of the hair follicle and the availability of liposomal preparations that selectively target the follicle, the topical introduction of genes seems feasible (Li and Hoffman, 1995), though the large amounts of genetic material and the need to re-apply the agent at intervals on a continued basis would make commercial use very expensive and impractical (Sawaya and Shapiro, 2000).

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CLINICAL REVIEWS

Evaluation and treatment of male and female Pattern hair loss

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Twenty years ago, there were neither specific treatments available for pattern hair loss nor full understanding of the pathophysiology of this common disorder. Male pattern hair loss (MPHL) [or androgenetic alopecia (AGA), male pattern baldness (MPB)] had been clearly recognized as an androgen-dependent hereditary disorder since the 1940's.[1] The principle of donor dominance was first appreciated at that time and led to the development of hair transplantation as a form of treatment.[2] However, it was not until recognition of the phenotype of individuals with the genetic deficiency of 5*a*- reductase (5*a*R),[3] the isolation of the two isoforms of 5*a*-reductase (5*a*R-1 and 5*a*R-2),[4,5] along with the documented utility of 5*a*-reductase inhibitors in male pattern baldness,[6] that the essential role of dihydrotestosterone (DHT) in male pattern hair loss was clearly established.

Much less is known about female pattern hair loss (FPHL) than MPHL, partly because of less recognizable patterns of hair loss in women, but also because of the common presence of other confounding factors.

The purpose of this review is to provide current information on the potential pathophysiology, clinical presentation, and histology of pattern hair loss in men and women. We also present our consensus opinion of an approach to the evaluation and treatment of pattern hair loss.

PATHOPHYSIOLOGY

A. In men

- MPHL is a common age-dependent trait: the frequency and severity increase with age so that at least 8O% of Caucasian men show at least some signs of MPHL by age 70.[7,8] Whether the thinning that occurs after age 50 to 60 is all androgen related or is secondary to some other factor related to aging is not entirely clear.
- Asian, Native American, and many men of African heritage have a decreased frequency of frontal hair loss and less extensive hair loss compared to Caucasians.[9-12]
- Male pattern hair loss is clearly androgen-dependent.
  - In Hamilton's studies, MPHL was absent in men castrated before puberty. However, MPHL developed in 4 of 12 male castrates treated with testosterone.[1]
  - MPHL has not been reported in Complete Androgen Insensitivity Syndrome in which there is failure of androgen receptor expression.[13]

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Disclaimer: None of the treatments discussed, particularly those that are not FDA-approved for male pattern hair loss or female pattern hair loss, should be construed as endorsements or specific recommendations for individual patients. These suggestions and opinions are meant to supply an evidence-based record of information from which a physician can make informed judgments about diagnosis and treatment.

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• Although testosterone is the major circulating androgen in men, the testosterone metabolite, dihydrotestosterone, plays a dominant role in MPHL.
— The conversion of testosterone to dihydrotestosterone is catalyzed by 5*a*R.
— There are two isoforms of 5*a*R with different tissue distributions and encoded by different genes.[5]
  — Type I 5*a*R is widely expressed but its physiological function is uncertain.
  — Type II 5*a*R is expressed in androgen-dependent tissues such as the prostate and hair follicle.
— MPHL is absent in men with genetic deficiency of Type II 5*a*R.[3,4]
— Treatment with finasteride, a selective inhibitor of Type II 5*a*R, slows the progression of MPHL and produces some regrowth of hair in about 2/3 of men.[6]
• The primary target of androgen action in the hair follicle is uncertain but there is some evidence that it is mesenchymally derived tissue (dermal papilla [DP] and dermal sheath [DS]).[14-20]
• Genetic factors predispose to MPHL, but their nature and the mode of inheritance is uncertain.
— Inheritance of MPHL is most likely polygenic.[21]
  — There is increased frequency of MPHL in sons of men with MPHL.[8,22] The maternal influence on MPHL is less well defined.
— The early onset of MPHL may be a marker of the carrier status of a gene responsible for polycystic ovarian syndrome in some women.[23] This gene has not been identified.
— Polymorphism in the androgen receptor gene is associated with MPHL, particularly early onset.[24] However, this does not explain the paternal effect in men with MPHL since the androgen receptor gene is located on the X chromosome and, therefore, inherited only from the mother.

B. In women
• As in men, the frequency and severity of FPHL increase with age.[25]
• The role of androgens in all cases of FPHL is less certain and the authors recommend the more general term 'female pattern hair loss' rather than the term androgenetic alopecia.[26]
• FPHL undoubtedly, but not necessarily, occurs in women with hyperandrogenemia.[27]
— These women with hyperandrogenemia may show a 'male' pattern of hair loss,
— These women typically have other signs of hyperandrogenism, eg, hirsutism and/or menstrual disturbance. Hyperandrogenism implies an increased expression of androgen-related conditions but does not require an absolute elevation of serum androgens.
— Women with pattern hair loss in the presence of signs of hyperandrogenism may respond to treatment with finasteride,[28] or cyproterone acetate.[29]
• But:
— The pattern of hair loss in women with FPHL is usually different from that seen in men with MPHL (see clinical findings below).
— Most women with FPHL show no other clinical or biochemical evidence of androgen excess.[27]
— The family histories of women with FPHL are not as straightforward as those of men with MPHL.[30]
— There was no response in postmenopausal women to treatment with finasteride[31] or in women without signs of androgen excess to cyproterone acetate.[29]

General
Whatever the etiology, the follicular changes in MPHL and FPHL appear identical, ie, there is a 'final common pathway' of follicular miniaturization. This includes:
• Progressive reduction in the duration of anagen.
• The prolongation of the latent period of the hair cycle[32] (not yet confirmed in women). Normally, anagen reasserts itself after a fixed period of telogen towards the end of which the hair is shed. The latent period is a period of persistent suspension of growth of the follicle after the hair shaft has been shed.
• Follicular miniaturization
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CLINICAL FINDINGS
A. In men
• Onset:
— May begin anytime post-puberty, usually by age 40.
— 14% of healthy boys aged 15-17 years old show early signs of MPHL. (Trancik RJ, Spindler JR, Rose S et al: Incidence of androgenetic alopecia in males 15-17 years of age. Poster presented at 3rd Intercontinental Meet-

ing of the Hair Research Societies, June 13-15, 2001, Tokyo, Japan.)

— Distribution: Central scalp (this encompasses the frontal, mid, and vertex scalp).[33]

• Pattern:

— Most common: Varying degrees of hair loss in the bitemporal, frontal, mid scalp, and vertex regions that generally fall into one of the Hamilton-Norwood patterns of hair loss.[34]

— Uncommon: Diffuse scalp hair loss or female pattern of hair loss with diffuse central scalp hair thinning.

• Hair pull: May be positive in active early hair loss in the central scalp but generally negative in longstanding hair loss. If there is concomitant telogen effluvium, the hair pull may be positive diffusely over scalp.

• Affected hairs: Miniaturization (finer, shorter hairs) and decreased hair density to the same degree in a given area of the scalp may lead to baldness (no hair) in that area.

• Scalp: Generally normal. Concomitant seborrheic dermatitis is common. If the patient has perifollicular erythema or hyperkeratosis, consider a cicatricial alopecia variant.[35] A scalp biopsy is recommended in the latter case.

• Associated Findings: A higher incidence of coronary artery disease (CAD) has been reported in men with MPHL.[36,37] In one study of 19,112 US male physicians,[36] the relative risk of CAD was 1.32 (95% CI, 1.10-1.59) for moderate vertex baldness and, although independent of age, hypertension, or increased cholesterol, was stronger in men with hypertension or high cholesterol.

• Family history: Commonly positive for MPHL on either side of the family but 20% of patients do not have a family history of MPHL.

B. In women

• Onset:

— May begin any time post menarche or adrenarche.

— Many women also first complain of hair loss in the 40-50-year-old age group: Whether this is an exacerbation of long standing FPHL which has not been previously diagnosed or is truly late onset FPHL is not clear. That these women do not respond to a Type II 5*a*R inhibitor raises questions about the androgen-dependence of this subset of FPHL.[31]

• Distribution: Central scalp + /— sides of scalp.

• Pattern:

— Tends to be one of two patterns in most women: Diffuse central thinning[38] or frontal accentuation ("Christmas tree" pattern).[26,39]

— Fronto-temporal recession/vertex loss, ie, "male pattern," is a third, but uncommon, pattern.

— Bitemporal thinning is commonly associated with, but not necessarily indicative of, FPHL.

— There is not usually any recession of the frontal hairline although the hairs on the frontal margin are commonly miniaturized, ie, finer and shorter

• Hair pull: May be positive in active early loss in the central scalp but generally negative in longstanding hair loss. If there is a concomitant telogen effluvium, the hair pull may be positive diffusely over the scalp.

• Affected hairs: Miniaturization is generally not as uniform nor as profound in specific scalp areas as that in MPHL, and hence, there are no regions of absolute baldness as with MPHL.

• Scalp: Generally normal. Concomitant seborrheic dermatitis is common. If the patient has perifollicular erythema or hyperkeratoses, consider a cicatricial alopecia variant.[35] A scalp biopsy is recommended in the latter case.

• Associated findings: Signs or symptoms of hyperandrogenism should he looked for, ie, hirsuitism, moderate to severe or treatment-refractory acne, irregular menses, infertility, and/or galactorrhea. Acanthosis nigricans is a marker for insulin resistance which is commonly associated hvperandrogenism.[40]

• Family history: Women with FPHL are less likely than men with MPHL to have a history of first-degree relatives with MPHL.[41]

EVALUATION

A. General

• It is important to exclude other causes of hair loss that may mimic pattern hair loss (PHL) since some treatments for PHL are selective (eg, finasteride in MPHL). It is also important to determine if there are other concomitant hair disorders whose untreated presence could ultimately affect the utility of the treatments used for PHL. (eg, iron deficiency in FPHL).[42] The differential diagnosis of PHL should include acute and chronic telogen effluvium, diffuse or reverse ophiasis alopecia areata, and early cicatricial alopecia.

B. In men

- Anabolic steroids or supplemental androgens may worsen PHL.
- Consider checking thyroid stimulating hormone (TSH) if the hair loss is diffuse and not localized exclusively to typical MPHL areas.
- Consider iron evaluation in men on a strictly vegetarian or otherwise deficient **diet** or where blood loss could be an issue.

C. In women

- Screening blood work is generally recommended in all women. In otherwise healthy women, check TSH and serum ferritin. Hypothyroidism may cause a telogen effluvium[43] and iron deficiency is speculated to both cause a telogen effluvium[44] and **to** interfere with the efficacy of treatment of FPHL.[42] Iron deficiency may be screened by two methods: serum ferritin or serum iron and total iron binding capacity (TIBC). A low serum ferritin is diagnostic of iron deficiency. However, depleted iron stores in patients with chronic disease may not be detected by serum ferritin measurements since ferritin is an acute phase reactant, and active inflammatory disorders, malignancy, and infections increase its synthesis and may, by its elevation in these situations,[45] give a false sense of normal iron stores. Some physicians prefer to have a sedimentation rate drawn with the ferritin to rule out falsely high or normal levels of ferritin in those with underlying active medical problems. If physicians elect to check serum iron and total iron binding capacity instead of ferritin, patients should not be taking concomitant iron-containing preparations (ie, multivitamins with iron or oral contraceptive pills [OCPs] containing iron) for at least 24 hours beforehand since exogenous iron can increase serum iron transiently but mask deficient marrow iron stores. Iron supplements taken for ≥3 weeks can falsely elevate ferritin levels in the face of iron deficiency. Iron deficiency is associated with low serum iron and relatively high total iron binding capacity and low percent saturation.
- Other screening tests may he indicated by history including a complete blood cell (CBC) and/or free thyroxine (T4).
- The majority of women with FPHL have no clinical or biochemical evidence of androgen excess.[27] However, a subset of women with FPHL does, and women with concomitant signs/symptoms of hirsuitism, moderate to severe and/or treatment- refractory adult acne, acanthosis nigricans, irregular menses, and or galactorrhea should he adequately screened for hvperandrogenemia. In these cases, blood tests should include:

1. Free and/or total testosterone +/- dehydroepiandrosterone sulfate (DHEAS) at a minimum. Tests ideally should be done off of OCP's since OCP's will inhibit both ovarian and adrenal sources of androgens.[46] If these tests are normal on OCP's, but the suspicion is high for underlying hyperandrogenemia, they should be repeated at least one month after cessation of OCP's.
2. If testosterone is greater than *2.5* X normal or >200 ng/dL, or DHEAS is greater than *2X* normal or >700 ug/dL in premenopausal or >400 ug/dL in postmenopausal women**,** a work-up for a tumor with radiographic tests should be undertaken.[47]
3. Consider checking serum prolactin if galactorrhea is present or if there is increased testosterone or free testosterone.
4. Consider screening for congenital adrenal hyperplasia **(**CAH) if testosterone or DHEAS is elevated. An early morning serum 17-OH progesterone during the follicular phase of the cycle (days 1-14) would be a reasonable screening test for the most common form of CAH, ie, 21-hydroxylase deficiency.[48] However, a serum 17-OH progesterone pre- and post-Cortrosyn (synthetic adrenocorticotropic hormone [ACTH] stimulation test is the most reliable way of screening for 21-hydroxylase deficiency. If either prolactin or 17-OH progesterone is increased, one may wish to refer the patient to an interested endocrinologist for further evaluation and treatment.

HISTOPATHOLOGY

A. Indications for biopsy

- Diagnosis:
  - —Males: Usually not necessary unless a female pattern of hair loss, diffuse hair loss, or scalp changes suggestive of cicatricial alopecia confuse the diagnosis.
  - —Females: Sometimes necessary to exclude chronic telogen effluvium, diffuse alopecia areata, or cicatricial hair loss such as early central centrifugal cicatricial alopecia seen commonly in African**i** American women.
- Site of biopsy: The preferred area for biopsy is the central scalp in an area representative of the hair loss

process. Biopsy should not be from bitemporal area as this region may have miniaturized hairs independent of MPHL or FPHL.

- Type of biopsy: A punch biopsy of less than 4 mm in diameter that follows the direction of the hair shafts and is taken deep into the subcutaneous fat where anagen hair bulbs are located is standard. Many dermatopathologists favor horizontal sectioning of biopsies.[49]
- Histologic diagnosis:[49-51]

1. The key change is miniaturization of terminal hairs into vellus-like hairs. This change is progressive over time. The same changes characterize both male and female pattern hair loss.
2. The percentage of telogen hairs increases from a normal of 5% - 10% to 15% - 20% on average with a corresponding decrease in the percentage of anagen hairs. The percentage of telogen hairs is slightly less in female pattern hair loss than in male pattern hair loss.
3. Horizontal sections permit accurate follicular counts of terminal and vellus and vellus-like hairs and characterization of terminal hairs as anagen, catagen, or telogen. Terminal hairs have hair shafts that are > 0.03 mm in diameter and thicker than the follicle's inner root sheath. Vellus or vellus-like (miniaturized) hairs have hair shafts that are $\leq$ 0.03 mm in diameter and thinner than the follicle's inner root sheath.
4. Vertical sections show a limited number of hair follicles but do allow one to estimate the proportion of anagen, catagen, and telogen hairs and terminal vs vellus or vellus-like hairs.
5. The ratio of terminal to vellus or vellus-Iike hair normally is 7:1. In PHL, the ratio decreases to 1.9:1 (both sexes combined) or 1.5:1 (males only), 2.2:1 (females only).[52] The amount of vellus or vellus-like hairs is slightly less in FPHL than in MPHL.
6. The total number of hairs per unit area is usually normal in PHL (normal being approximately 240-400 hairs/cm_ or 30-50 hairs per 4 mm punch biopsy in normal adults)[52,53] but may be reduced in severe baldness or in elderly patients
7. A perifollicular infiltrate, predominantly lymphohistiocytic, may be present in pattern hair loss, around the upper or lower follicle. The prognostic implications of this finding are uncertain at this time.
8. Perifollicular fibrosis, usually comprising concentric layers of collagen deposition may be present in pattern hair loss around the upper and lower follicle. This may have negative implications for potential regrowth although further data are needed to corroborate this.

TREATMENT

A. General principles

- The diagnosis should be confirmed. Some treatments are specific to the pathophysiology of PHL, and others are nonspecific hair growth promoters.
- Patients should avoid hair care products likely to damage scalp/hair. This is particularly important African American Women
- Patients should maintain an adequate diet, especially one with adequate protein. The National Institutes of Health (NIH)) recommended daily allowance for protein is 0.35 gm/lb or 0.8 gm/kg, which translates into 45 grams for a 150-lb. person.
- Topical medications work only where the medication is applied; therefore, the entire area at risk of loss (the top of the scalp) should be treated with a given topical agent.
- If possible, any drugs that could negatively affect hair growth should be stopped and alternative substitutes made. Although certain drugs are more commonly associated with hair loss than others, any drug can potentially cause a telogen effluvium. Medications for which hair Ioss is a common potential side effect include retinoids,. cytotoxic agents, and anticoagulants
- Treat any underlying scalp disorder such its seborrheic dermatitis or scalp psoriasis as these conditions can affect the ability to use topical treatments for hair loss without irritation.

B. Medical treatment for men

GENERAL

- Currently, only finasteride 1 mg and minoxidil topical solution (2% and 5%) are FDA-approved for the treatment of male pattern hair loss.
- Both drugs retard further thinning and increase scalp coverage. However, in many patients, the main perceived response may be maintenance of current hair density.

- Neither drug restores all the lost hair. Neither drug is able to reverse total baldness.
- Both drugs require chronic use to maintain effectiveness. If treatment is discontinued the effects of the drug are lost over several months, and the hair density will evolve into what it would have been without treatment.
- Treatment shouId be used for 12 months before making a decision about efficacy although benefit may be seen sooner.

Finasteride (1 MG ORAL DAILY)

- FDA-approved for men ≥ 18 years old.
- Mode of action:
  - Competitive inhibitor of Type II 5*a*R that decreases the conversion of testosterone (T) to DHT. DHT serum and scalp is decreased ~2/3 with treatment.[54]
- Efficacy:
  - — Target area hair counts (TAHC) are generally used to assess efficacy in clinical trials of MPHL. TAHC's are circular target areas 1 cm to 1 inch in diameter typically at the interior leading edge of the vertex balding area where the terminal, non-vellus, or visible hairs are counted pre- and post-treatment.
  - — Target area hair counts increase over the first year and peak by ~ 12 months: In men age 18-41, hair counts increased 16.9/cm_ for those on 1 mg finasteride vs - 4.1/cm_ for those on placebo.[6]
  - — By expert panel review of global photographs, hair growth continues to improve for at least the first 24 months of treatment as the hairs grow longer and thicker. In men aged 18- 41, ~ 50% of men showed an increase in hair growth by 1 year, and 66% by 2 years on finasteride, compared to 7% and 7% at both 1 and 2 years respectively for placebo.[6] In men aged 41-60, 39% on finasteride versus 3% on placebo showed increased hair growth at 2 years.[55]
  - — 5-year placebo controlled trials using both hair counts and expert panel review of global photographs as endpoints confirm that continued use of finasteride helps to maintain this effect and to slow further hair loss.[56]
  - — If treatment with finasteride is discontinued, any positive effect on hair growth will be lost in 12 months.[6]
- Safety
  - — No known drug interactions.
  - — No effects on liver, kidney, bone marrow, or bone or serum lipids.
  - — No effect on spermatogenesis.
  - — Reversible sexually-related side effects (decreased libido, erectile dysfunction, decreased ejaculate volume) were seen in 1.8% of men aged 18- 41 versus 1.1% of those on placebo.[6] In older men aged 41-60, sexually-related side effects were seen in 8.7% on finasteride vs 5.1% on placebo.[54] These side effects often resolve during continued treatment or within days to weeks after treatment with finasteride is discontinued.
  - — The level of finasteride in semen of men taking finasteride is very low and semen from a man taking finasteride poses no risk to a pregnant woman or to her fetus.[57]
  - — Reduction in prostate specific antigen (PSA) is physiologically based on the effect of decreased DHT on the prostate. Recommendation is that any PSA test value should be doubled for any man taking finasteride to compensate for the effect of the drug.[58,59]
  - — Recent data from a long-term (7 year) trial of 18,882 men greater than or equal to 55 years old with normal digital rectal examination and less than or equal to 3.0 ng/ml serum PSA who took 5 mg finasteride (5X the standard dose recommended for MPHL) vs placebo revealed a 25% decrease in prostate cancer for those on finasteride (803 on finasteride vs 1147 on placebo).60 However, 6.4% of men on finasteride developed histologically high grade cancer (defined as Gleason score 7-10) vs 5.1% of those on placebo. This study only monitored changes in the number of prostate cancers and histologic subtype but did not address the biological aggressiveness of the tumors or outcome. Potentia1 hypotheses for the findings include that: (a) finasteride may selectively inhibit low grade prostate tumors, (b) low DHT may induce histologic changes that mimic high grade disease, or (c) low DHT may induce higher grade prostate cancers. Further research and long-term observation of men taking finasteride 1 mg needs to be done on this issue.

MINOXIDIL TOPICAl. SOLUTION 2% AND 5%

- FDA-approved for men > 18 years old. Adolescents have been treated with topical minoxidil solution without any additional problems (Trancik RJ, Spindler JR, Cuddihy RV, et al.: Clinician survey evaluating minoxidil topical solution in the treatment of androgenetic alopecia in patients under 18 years of age. Poster presented at 3rd Intercontinental Meeting of the Hair Research Societies, June 13-15, 2001. Tokyo, Japan).
- Mode of action:

— Increases duration of anagen and enlarges miniaturized follicles.

— Potassium channel opener and vasodilator. The precise mechanism of action is unknown but appears independent of vasodilation.61

• Application: 1 mL twice daily to dry scalp, preferably using a dropper application. Topical minoxidil solution requires approximately 1 hour for absorption. If the patient shampoos or the scalp becomes wet, eg, from excessive sweating or rain, the medication should be re-applied. If gel or hair spray is used, the medication should be applied first so that absorption is not affected.

• Efficacy:

— Target area hair counts and global photographs confirm a significant increase in hair density.62 The hair growth appears to peak at 16 weeks.62 The placebo-controlled trials of both target area hair counts and expert panel review of global photographs at 1 year 62 and hair weight studies over 2 years 63 confirm that continued use of topical minoxidil solution helps to maintain this effect and to slow further loss.

— 5% topical minoxidil solution is superior to 2% topical minoxidil solution by target hair counts, expert panel review of global photographs,62 and hair weight studies in men with MPHL.63 Target area hair count increases are

18.6/cm^2 for 5% topical minoxidil solution, 12.7/cm^2 for 2% topical minoxidil solution and 3.9/cm^2 for placebo at 48 weeks. Expert panel review of global photographs show increased growth at 1 year in 57,9% on 5% topical minoxidil solution**,** 40.8% on 2**%** topical minoxidil solution, and 23.2% on placebo.[62]

— If treatment is discontinued. any positive effect on hair growth will be lost in 4-6 months.[64]

— Topical minoxidil solution may initially cause a telogen effluvium beginning 2-8 weeks after treatment initiation. This temporary shedding, resulting from the minoxidil initiated release of telogen hairs (‘‘exogen’’) as anagen promotion begins, is self-limiting with continued treatment and should not be a cause for concern. Patients should, however, be forewarned so that treatment is not interrupted.

▪ Safety: Adverse effects are mainly dermatologic.[62]

— Scalp irritation, including dryness, scaling, itching, and/or redness, may occur; these are more common with the 5% topical minoxidil solution than the 2% topical minoxidil solution.

– Allergic contact dermatitis is uncommon.[56] Patch test kits are available from Pfizer and may help to sort out whether a rash is an irritant or allergic contact dermatitis and whether it is related to minoxidil or propylene glycol.

• Combination treatment of finasteride and topical minoxidil

— There have been no well-controlled studies in humans. A study in the stumptailed macacque, an animal model for pattern hair loss in both sexes, showed art additive effect when both drugs were used concurrently.[65]

— Men who wish to switch from treatment with one of these agents to the other should continue using the original medication in addition to the new agent for at least 3 months before discontinuing it. The cross over period is needed to provide time for the newer drug to reach a point of effectiveness to avoid excess shedding.

C. Medical treatment for women

WOMEN WITH OR WITHOUT HYPERANDROGENISM:

• If women are on hormone replacement therapy or an OCP, the dose and type should be stabilized, Over-the-counter DHEA or testosterone in hormone replacement therapies should be avoided. In this way, women with FPHL will minimize external additions to any potential underlying androgen sensitivity.

• Minoxidil Topical Solution:

Efficacy:

— currently. only 2% topical minoxidil solution is FDA-approved for the treatment of ‘‘women with thinning hair.’’[66]

— 5% topical minoxidil solution, although not currently FDA—approved for use in women, has been evaluated in women with FPHL and was found to be significantly more effective than placebo by both target area hair counts and subject assessment.[67] There was a trend towards superior efficacy of 5% topical minoxidil solution over 2% topical minoxidil solution but this was not consistently statistically significant. Target area hair counts

at 48 weeks showed a change from baseline of 24.5/cm_, 20.7/cm_, and 9.4/cm^2 in the 5% topical minoxidil solution, 2% topical minoxidil solution, and placebo group respectively. The sensitivity of target area hair counts as a primary endpoint in FPHL has been questioned.[33]

—Treatment should be used for 12 months before making a decision about efficacy although benefit may be seen sooner.

—Topical minoxidil solution works in those women with FPHL both with and without hyperandrogenism and in young and old, pre- a and postmenopausal women alike.

Safety:

—Either 2% or 5%, topical minoxidil solution appears safe to use in women with FHPL, with the only additional risk of the 5% topical minoxidil solution over the 2% topical minoxidil solution being a higher incidence of facial hypertrichosis. The hypertrichosis tends to occur over the cheeks and forehead as vellus, not terminal hair and disappears within 4 months of stopping the drug. Although this may he related to inadvertent spreading to the face after local application to the scalp, this may also be a result of hypersensitivity to low levels of systemic absorption of minoxidil. Other local side effects are the same as in men.

WOMEN WITH HYPERANDROGENISM

- Hvperandrogenism is synonymous with excessive secretion of androgens[68] the indirect evidence of which is the existence of hirsuitism, severe or treatment refractory acne and/or irregular menses (the latter in a woman of childbearing potential off of OCP's), and/or elevation of serum testosterone, free testosterone, or DHEAS. Less than 40% of women FPHL have hyperandrogenism[27] but this population, with clear-cut evidence of androgen hypersensitivity or overproduction, may

respond differently to drugs that block the production or effect of androgens than those women with FPHL and no hyperandrogenism.

- Antiandrogens and 5*a*—reductase inhibitors
  - There are few studies evaluating the effect of antiandrgens or 5*a*R inhibitor in FPHL and only one that is large and placebo—controlled**.** Most studies showing efficacy of these agents have been done in women with hyperandrogenism, particularly those with hirsuitism. Studies of these agents in women with FPHL who do not have overt hyperandrogenism have not specifically shown proven efficacy. In the United States, all of these agents are used off-label for the treatment of hirsutism or female pattern hair loss.

—Since all antiandrogens or 5*a*R inhibitors may cause feminization of a male fetus, all women of childbearing potential should use effective means of contraception while taking any of these drugs. OCPs have the additional advantage of also lowering serum androgens. Women of childbearing potential who use an antiandrogen or 5*a*—reductase inhibitor should be cautioned to stop the medication and call their doctor if their menses are late.

—If of childbearing potential and on an OCP for at least 1 month with a negative pregnancy test, or if of non-childbearing potential, one may try either:

—Spironolactone 100 - 200 mg per day.

1. Only small, uncontrolled studies with spironolactone in FPHL have been published but they support efficacy in the subset of FPHL with hyperandrogenism. [69]
2. For safety purposes, one should check serum potassium at baseline and 1 month after beginning treatment since hyperkalemia is a rare side effect. Patients should keep well hydrated.

—Finasteride 1-1.25 mg per day

1. In a well-controlled study, finasteride I mg per day, was not shown to be useful in post-menopausal women with FPHL.[31] These subjects were not specifically stratified for hyperandrogenism.
2. Some positive reports in women with hyperandrogenism treated with 1.25 mg per day have emerged.[28]
3. There are no anticipated side effects and no blood tests are necessary.

—Cvproterene acetate:

1. 100 mg days 5-15 combined with 50 ug ethinyl estradiol on days 5-25 of the menstrual cycle appears most useful.[70]
2. Only one well-controlled study has been done with FPHL and this proves the value of cyproterone acetate

in women with hyperandrogenism only.[29]

3. Diane (2 mg cyproterene acetate days 5-15 and 50 ug ethinyI estradiol days 5-25 of the menstrual cycle) appears to be less effective in hair loss. [71]

4. No specific blood tests are necessary.

D. Cosmetic aids

- Nonmedical approaches can provide cosmetic relief to men and women with thinning hair if medical treatments are not indicated, not effective, or not desired by the patient. They can also be used as adjuvant therapy if medical or surgical treatments are used.
- Tinted powders, lotions, and hair sprays can all provide a cosmetic covering of the scalp in areas of scalp hair thinning and can be useful in camouflaging it.
- Wigs. hair pieces, and hair extensions can be used to cover a thinning scalp. Advances in the technology of these prostheses have made their use much more acceptable.

E. Surgical treatment[72-74]

HAIR TRANSPLANTS

. Criteria for assessing male candidates:

— Age:

— Patients over the age of 25 years are preferable. The predictive value of future hair loss is much lower for individuals between the ages of 15 and 25 years of age and surgery in this young group of men may result in misplaced hairlines or an unnatural appearance 20 or 30 years later. Young men with early hair loss (Hamilton-Norwood I and II patterns) already have enough hair for facial framing and will receive limited aesthetic benefit from surgery.

- Degree of frontal and vertex hair loss:

Vertex baldness is a progressive process and does not become "stable with time'', and therefore, hair transplantation of the vertex should be approached with extreme caution**.** Ideal candidates are those with just frontal and mid-frontal hair loss. When frontal baldness is corrected, this creates the most dramatic positive change in appearance.

- Density of donor area should he adequate:

Patients with <40 follicular units/cm_ in the donor area are considered poor candidates.

- Hair caliber and color: Thicker hair shafts (>60-70 microns) demonstrate better coverage

compared to finer hair. Lightcr colored hair in Caucasians gives a more natural look compared to dark colored hair since the contrast between hair and skin is not as apparent.

- Criteria for assessing female candidates:

— Women with mild female pattern alopecia (early Ludwig I) arc not optimal surgical candidates since differences in pre-transplanted scalp vs. post-transplanted scalp are difficult to appreciate.

— Those with diffuse unpatterned alopecia are poor surgical candidates for the obvious reason that the entire scalp is suffering hair loss, thus, the donor area is of limited value as it is also susceptible to loss.

— The ideal female patients for hair transplantation are those with high-density donor hair and extensive hair loss or thinning of the frontal scalp.

- Number of sessions:

Experienced surgical teams can create significant coverage in one to two sessions with dense packing of higher number of grafts (1000-2000) being performed per session. Final results are usually seen 5-6 months after the procedure, and thus, timing between sessions, if needed, Is usually a minimum of 6 months.

- Complications:

— Facial edema, scalp erythema, and recipient site crusts of the scalp are common but usually resolve within 3-7 days although crusting may persist a few additional days.

— Other possible complications of hair transplants include nausea and vomiting, post operative bleeding (less than 0.5%), infection (less than 05%), excessive swelling (5%), temporary headache, temporary numbness of the scalp, abnormal scarring around the grafts (less than 1%), poor growth of grafts, fainting (less than 1%), folliculitis, keloid formation, neuroma, persistent scalp pain, telogen effluvium, and arterio-venous fistula formation.

SCALP REDUCTIONS

- Description:

— Hair-bearing skin is brought closer together by removing the center scalp affected by the alopecia.

— Not commonly performed currently.

— Many different designs employed in excising the balding area.

— Reductions may be performed in conjunction with hair transplantation to the remaining bald scalp for a more optimum result.

- Potential complications:

— The efficacy diminishes over time due to the unpredictable progression of hair loss in any given individual.

— Excision scars become noticeable over time.

— The scar may potentially widen secondary to stretching of adjacent scalp skin.

— Usually more than one scalp reduction is necessary to effectively address a person's baldness.

Adjunctive medical therapy with surgery

The use of finasteride and/or topical minoxidil may stabilize underlying hair loss therefore necessitating less donor harvesting and less scalp reductions. This will also allow the patient to maintain a more natural appearance over time.

CONCLUSION

Although the clinical aspects of pattern hair loss are well-recognized in both men and women and the role of DHT and MPHL is well documented, much remains to be determined regarding the genetics and pathophysiology of these common conditions. There are effective treatments, either medical or surgical, available currently for some men and women with pattern hair loss, but clearly further treatment options arc desired, particularly for women with FPHI..

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Constituents of *Lepidium meyenii* 'maca'

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Abstract

The tubers of *Lepidium meyenii* contain the benzylated derivative of 1,2-dihydro-*N*-hydroxypyridine, named macaridine, together with the benzylated alkamides (macamides), *N*-benzyl-5-oxo-6*E*,8*E*-octadecadienamide and *N*-benzylhexadecanamide, as well as the acyclic keto acid, 5-oxo-6*E*,8*E*-octadecadienoic acid. The structure elucidation of the isolated compounds was based primarily on 1D and 2D NMR spectroscopic analyses, including ^{1}H–^{1}H COSY, ^{1}H–^{13}C HMQC, ^{1}H–^{13}C HMBC and ^{1}H–^{1}H NOESY experiments, as well as from ^{1}H–^{15}N NMR HMBC correlations for macaridine and *N*-benzylhexadecanamide. © 2002 Published by Elsevier Science Ltd.

Keywords: *Lepidium meyenii*; Brassicaceae; 1,2-Dihydro-*N*-hydroxypyridine; Macaridine; Macamide; *N*-Benzyl-5-oxo-6*E*,8*E*-octadecadienamide; *N*-Benzylhexadecanamide; 5-Oxo-6*E*,8*E*-octadecadienoic acid; 2D NMR; ^{1}H–^{15}N NMR

1. Introduction

Lepidium meyenii Walp. (Brassicaceae), commonly known as 'maca', is a nutritionally valuable native Peruvian plant that is used in the Andean diet (Leon, 1964). This plant was domesticated at least two centuries ago in the Andean mountains, where natives used its tubers as food and as a folk medicine. *L. meyenii* is known to contain valuable nutritional ingredients (Dini et al., 1994) and is used locally for the enhancement of fertility and sexual behavior in men and women, and as a traditional remedy of menopausal symptoms. The aphrodisiac activity of *L. meyenii* after oral administration in mice has recently been reported by Zheng et al. (2000). Earlier chemical work on the roots of this plant yielded mainly macaenes, macamides (alkamides), fatty acids, sterols and benzyl isothiocyanate (Zheng et al., 2000). However, other species of the genus *Lepidium* exhibit the presence of flavonoids, flavonoid glycosides (Fursa et al., 1970; KurKin et al., 1981) and alkaloids, including the *bis*-benzyl imidazole derivatives from *L. sativum* (Maier et al., 1998).

Several 'maca' dietary supplements[1] are currently available in the United States for the nutritional supplement of various sexual dysfunctions in men and women. As part of our continuing program to isolate marker compounds from traditional medicine and dietary supplements (Ganzera et al., 2001; Muhammad et al., 2001 a,b), the present study deals with the isolation and characterization of a 1,2-dihydro-*N*-hydroxypyridine derivative, macaridine (**1**), together with the hitherto unreported constituents *N*-benzyl-5-oxo-6*E*,8*E*-octadecadienamide (**2**), *N*-benzylhexadecanamide (**3**) and 5-oxo-6*E*,8*E*-octadecadienoic acid (**4**), from the tubers of *L. meyenii*.

2. Results and discussion

The petroleum ether extract of *L. meyenii* tubers was subjected to column chromatography (CC), followed by a short flash-CC and centrifugal preparative TLC (see

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[1] Maca Pure™ (Patent pending), Pure World Botanicals, Inc., 375 Huyler Street, South Hackensack, NJ 07606, USA, Web address <http://www.madis.com/news/macapure_spec.html>; Maca 750™, Medicine Plants, Web address: <http://www.maca750.com>.

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Experimental) to give compounds **1**–**4**. Compound **1**, analyzed for $C_{13}H_{13}NO_2$ by HRMS, gave a light pink color with aqueous $FeCl_3$, but was inactive with Dragendorff's reagent. The UV spectrum demonstrated α,β-unsaturated carbonyl and benzyl chromophores at λ_{max} 294 and 210 nm, respectively, and the IR spectrum showed hydroxyl, conjugated aldehyde and aromatic absorption bands [ν_{max} 3385 (*br.*), 1658, 781 and 725 cm^{-1}]. The ^1H NMR spectrum exhibited a deshielded proton at δ 9.52 (1H, *s*; $\delta_{C\text{-}8}$ 180.2, *d*) for an aldehyde group, two olefinic protons at δ 6.29 and 6.94 (each *d*, $J_{=}4$ Hz; $\delta_{C\text{-}6}$ 111.2, $\delta_{C\text{-}5}$ 124.8) for a *cis*-disubstituted double bond and five aromatic protons (δ 6.98, 2H, *d*, $J=7.1$ Hz; 7.22-7.29, 3H, *m*; $\delta_{C\text{-}9}$ 138.2, $\delta_{C\text{-}10,14}$ 126.2, $\delta_{C\text{-}11,13}$ 129.1, $\delta_{C\text{-}12}$ 128.0) for a monosubstituted benzene ring. The ^{13}C NMR spectrum revealed two additional quaternary carbons at $\delta_{C\text{-}3}$ 142.5 and $\delta_{C\text{-}4}$ 133.2, accounting for a C-3(4)-tetrasubstituted double bond. In addition, the ^1H NMR spectrum demonstrated two 2H singlets at δ 4.54 ($\delta_{C\text{-}2}$ 57.0) and 5.73 ($\delta_{C\text{-}8}$ 48.9), indicating the presence of two sets of isolated methylene protons for –N–$\underline{CH_2}$–and C_6H_5–$\underline{CH_2}$– groups, respectively. The deshielding of the C-8–CH_2– protons was due to benzylic and allylic groups, as well as the anisotropic effect of C-7 carbonyl group. The ^{13}C NMR chemical shift value for the methylene carbon between nitrogen and oxygen atoms (–N–$\underline{CH_2}$–O–) was found to be highly deshielded (δ_C 80–83) (Linde et al., 1978; Hatfield and Maciel, 1987) compared to that observed for an *N*-methylene group ($\delta_{C\text{-}2}$ 57.0), which ruled out the possibility of an alternative dihydrooxazepine-type base structure. The ^1H–^{15}N NMR HMBC experiment established the presence of a single nitrogen atom at δ_N 159.7, suggesting the presence of an hydroxylamino group (–CH_2–$\underline{N(OH)}$–R), rather than an N–H group. (Hatfield and Maciel, 1987; Witanowski et al., 1993; Hadden et al., 1999) in a 1,2-dihydropyridine base structure. The presence of an hydroxylamino group was also supported by the HRMS using collision induced dissociation in the ESI source, which clearly demonstrated a strong fragment ion at *m*/*z* 198.0918 ($[C_{13}H_{12}NO]^+$, $[M-OH]^+$, calc. for 198.0913) due to the loss of OH^- ion, while no such fragment ion was observed under standard conditions. Furthermore, the lack of an NH proton and oxygenated carbon in the ^1H and ^{13}C NMR spectra, respectively, as well as the absence of a one bond correlation between the nitrogen atom and the NH proton in the ^1H–^{15}N NMR HMBC spectrum (with no low pass filter) could only suggest the presence of a hydroxyl group at the N-1 position. The above spectral data suggested the presence of benzyl and formyl groups in a 1,2-dihydro-*N*-hydroxypyridine nucleus and the placement of the substituents was established by gradient DQF-COSY, HMQC, gradient ^1H–^{13}C HMBC and ^1H–^{15}N HMBC NMR experiments.

The COSY and HMQC experiments established the systems –C–CH=CH–R– and C_6–H_5–, while the HMBC (Fig. 1) showed three-bond correlations between $\delta_{C\text{-}7}$ 180.2 and H-5, $\delta_{C\text{-}3}$ 142.5 and H-7, $\delta_{C\text{-}4}$ 133.2 and H_2-8, $\delta_{C\text{-}10,14}$ 126.5 and H_2-8, and $\delta_{C\text{-}2}$ 57.0 and H-6, confirming the relative placements of the *N*-methylene, benzyl, for-

Table 1
^1H NMR spectral data and coupling constants (in parentheses, in Hz) for compounds **2**–**4**[a]

Protons	**2**	**3**	**4**
2	2.17 *m*	2.11 *t* (9.3)	2.29 *m*
3	1.61 *br m*	1.55 *m*	1.57 *br m*
4	2.50 *br t* (7.3)	–	2.49 *br t* (7.0)
6	6.04 *d* (15.4)	–	6.03 *d* (15.5)
7	7.09 *dd* (3.0, 9.7, 15.4)	–	7.07 *dd* (2.8, 8.8, 15.5)
8	6.14 *m*	–	6.14 *m*
9	6.12 *m*	–	6.12 *m*
10	2.13 *m*	–	2.13 *m*
15	–	1.17 *m*[b]	–
16	–	0.81 *t* (6.9)	–
17	1.24 *m*[b]	–	1.26 *m*[b]
18	0.87 *t* (7.0)	–	0.85 *t* (7.0)
1′	4.41 *d* (5.6)	4.31 *d* (7.0)	–
3′	7.24 *d* (8.4)	7.17 *d* (8.0)	–
4′	7.30 *m*	7.22 *m*	–
5′	7.30 *m*	7.22 *m*	–
6′	7.30 *m*	7.22 *m*	–
7′	7.24 *d* (8.4)	7.17 *d* (8.0)	–
Other protons	1.29–1.43 *m*	1.18 *br s*, 1.94 *m*	1.21–1.58 *m*
	12H (H-11–H-16)	22H (H-4–H-14)	12H (H-11–H-16)
N—H	5.76 *br s*	6.03 *br s*	–

[a] Spectra for **2**–**4** were recorded at 500 MHz in $CDCl_3$.
[b] Superimposed with other CH_2 protons.

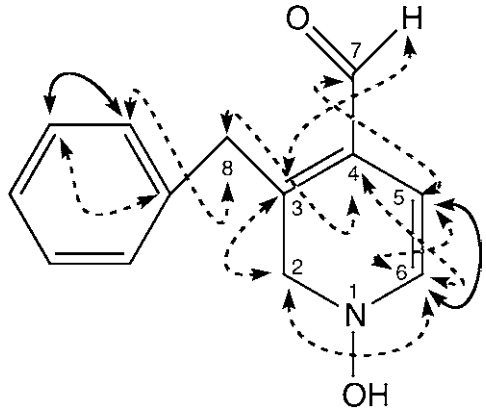
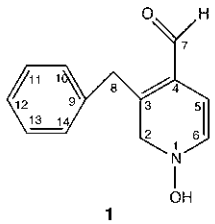


Fig. 1. 2D NMR ^{1}H–^{13}C HMBC (broken lines) and COSY (solid lines) correlations for compound **1**.

myl and olefinic substituents at C-2–C-4 and C-5(6) positions, respectively. The HMBC also showed correlations between $\delta_{C\text{-}3}$ 142.5 and $\delta_{H\text{-}2}$ 4.54, as well as correlations between $\delta_{C\text{-}4}$ 133.2 and $\delta_{H\text{-}6}$ 6.29. This establishes the position of $\delta_{C\text{-}2}$ 57.0 between the nitrogen atom and C-3. The assignment of the nitrogen atom at the N-1 position was confirmed using an ^{1}H–^{15}N HMBC experiment which showed ^{2}J correlations between the signals at $\delta_{N\text{-}1}$ 159.7, $\delta_{H\text{-}2}$ 4.54 and $\delta_{H\text{-}6}$ 6.29, ^{3}J correlations between $\delta_{N\text{-}1}$ 159.7 and $\delta_{H\text{-}5}$ 6.94, ^{4}J correlations between $\delta_{N\text{-}1}$ 159.7 and $\delta_{H\text{-}8}$ 5.73; as well as ^{5}J correlations through double bonds with $\delta_{H\text{-}7}$ 9.52. From the foregoing data the structure of **1**, named macaridine, was assigned as shown.



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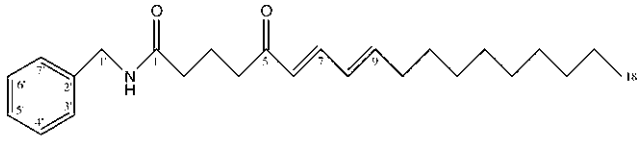

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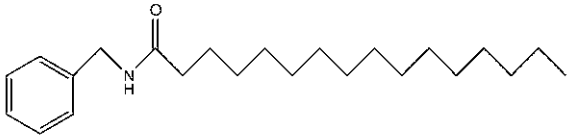

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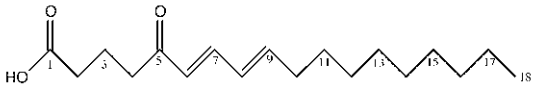

4

Alkamides **2** and **3** analyzed for the molecular formulas $C_{25}H_{37}NO_2$ and $C_{23}H_{39}NO$, respectively, by HRMS. The alkamides were homogenous on TLC, but were inactive with Dragendorff's reagent. The UV spectrum of **2** showed chromophores for a benzyl group and an α,β-unsaturated ketone (λ_{max} 210, 274 nm), and the IR spectrum exhibited absorption bands at ν_{max} 3311 and 1638 cm^{-1}, for N–H and carbonyl group(s), respectively. The NMR spectra revealed a carbonyl (δ_C 201.4), an amide carbonyl (δ_C 173.3) and a monosubstituted benzene ring (Tables 1 and 2), as well as two disubstituted double bonds (δ_C 127.9, 143.4, 131.7, 146.1; each *d*; C-6–C-9, respectively), indicating that compound **2** is a benzylamide of an oxo-octadecadienoic acid. The ^{1}H NMR spectrum exhibited two *trans*-coupled olefinic protons at δ 7.09 (*ddd*, $J = 3.0$, 9.7, 15.4 Hz, H-7) and 6.04 (*d*, $J = 15.4$ Hz, H-6), two other olefinic protons between δ 6.14 and 6.12 (*m*, H-8 and H-9), a primary methyl group at δ 0.87 (*t*, $J = 7.0$, H-18), as well as 22 protons between δ 1.29–2.43, attributed to eleven methylene groups. Due to the complexity of the H-8 and H-9 signals, the coupling constants could not be established. A 2D NMR ^{1}H–^{1}H COSY experiment of **2** established the diene system –CH=CH–CH=CH–CH_2–, which was further substantiated by a series of double resonance experiments. Thus, irradiation of the protons at δ 6.12 and 6.14 (H-8 and H-9) resulted in a doublet at δ 7.09 ($J = 13$ Hz, H-7), confirming the presence of a *trans*-olefin at the C-6(7) position. The geometry of

Table 2
^{13}C NMR spectral data for compounds **2**–**4**[a]

Carbon	**2**	**3**	**4**
1	173.3 *s*[b]	173.3 *s*	179.5 *s*
2	37.1 *t*	36.9 *t*	34.3 *t*
3	24.7 *t*	–	24.7 *t*
4	40.8 *t*	–	40.8 *t*
5	201.4 *s*	–	201.5 *s*
6	127.9 *d*	–	128.2 *d*
7	143.4 *d*	–	143.4 *d*
8	131.7 *d*	–	130.8 *d*
9	146.1 *d*	–	146.0 *d*
10	33.5 *t*	–	33.4 *t*
15	–	22.8 *t*	–
16	–	14.3 *q*	–
17	22.8 *t*	–	22.7 *t*
18	14.4 *q*	–	14.3 *q*
1′	44.0 *t*	43.7 *t*	–
2′	138.8 *s*	138.6 *s*	–
3′	128.2 *d*	127.9 *d*	–
4′	129.2 *d*	128.8 *d*	–
5′	129.1 *d*	127.5 *d*	–
6′	129.2 *d*	128.8 *d*	–
7′	128.2 *d*	127.9 *d*	–
Other carbon	25.0–31.7 (6 *t*) 6×CH_2	22.8–36.9 (11 *t*) 11×CH_2	25.0–31.7 (6 *t*) 6×CH_2

[a] Spectra for **2**–**4** were recorded at 125 MHz in $CDCl_3$.
[b] Multiplicities were determined by DEPT 135°, also aided by 2D NMR COSY and HMQC experiments.

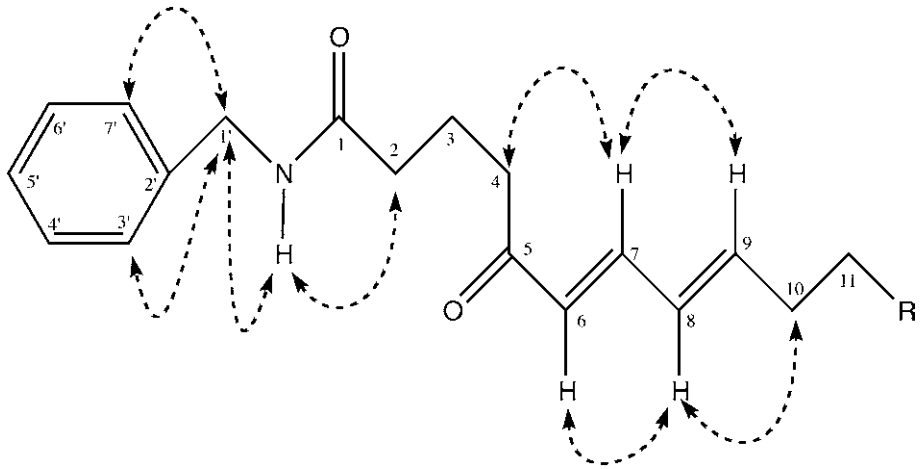

Fig. 2. 2D NMR ^{1}H–^{1}H NOESY correlations for compound **2**.

the C-8(9) double bond was established as *trans* by using 2D NMR ^{1}H–^{1}H NOESY experiment (vide infra; Fig. 2). Furthermore, the ^{1}H NMR spectrum revealed five aromatic protons (δ 7.24, 2H, *d*, $J=8.4$ Hz, H-3′,7′; 7.30, 3H, *m*, H-4′-6′), *N*-benzyl methylene protons at δ 4.41 (2H, *d*, $J=5.6$ Hz, H-1′) and a broad one proton singlet at δ 5.76, attributable to an N–H group. These spectral data are in close agreement with those observed for *N*-benzylhexadecanamide (**3**) (Tables 1 and 2). Thus, a close comparison of the ^{1}H and ^{13}C NMR spectral data of **2** with those of **3** led to the conclusion that indeed compound **2** was a benzylated alkamide of oxo-octadecadienoic acid.

The geometry of the double bonds at C-6(7) and C-8(9) was inferred from 2D NMR ^{1}H–^{1}H NOESY experiments, which showed cross peaks between H-4 (δ 2.50) and H-7 (δ 7.09). On the other hand, no NOESY correlation was observed between H-7 and H-10 (δ 2.13), while H-7 was correlated with H-9, suggesting *E* configurations for both the olefins [at C-6(7) and C-8(9)]. Furthermore, the NOESY spectrum showed cross peaks between H-6 (δ 6.04) and H-8 (centered at δ 6.14), the latter proton being correlated with H-10 (δ 2.13), thereby confirming the assignment of a *trans*-C-8(9) olefin. Other key NOESY correlations are depicted in Fig. 2. Molecular modeling[2] indicated that the NOESY correlation between H-7 and H-9 (2.4 Å), and H-8 and H-10 (2.3 Å) are consistent with a *trans* C-8(9) double bond. From the foregoing data alkamide **2** was assigned as *N*-benzyl-5-oxo-6*E*,8*E*-octadecadienamide.

The structure of alkamide **3** was unambiguously established by rigorous 2D NMR COSY, HMQC, and HMBC experiments. In addition, the placement of the secondary amide group system (–CH_2–NH–CO–CH_2–) in **3** was confirmed by a ^{1}H–^{15}N NMR HMBC experiment, which showed the ^{1}J, ^{2}J and ^{3}J correlations between the signals at δ_N 118.6 (–NH–CO–) and $\delta_{N\text{-}H}$ 6.03, $\delta_{H\text{-}1'}$ 4.31, $\delta_{H\text{-}2}$ 2.11, respectively.

Compound (**4**) displayed the molecular formula $C_{18}H_{30}O_3$ from its HRMS, indicating four degrees of unsaturation. The ^{1}H and ^{13}C NMR spectral data (Tables 1 and 2) of **4** were found to be generally similar to those observed for **2**, except for the differences associated with the absence of an *N*-benzyl group at C-1. Its UV spectrum had a chromophore expected for an α, β-unsaturated ketone (λ_{max} 274 nm), and the IR spectrum showed a strong and broad carbonyl absorption band (ν_{max} 1708 cm^{-1}). The^{13}C NMR spectrum revealed carbonyl (δ_C 201.5) and carboxylic acid (δ_C179.5) groups, as well as two disubstituted double bonds (δ_C 128.2, 143.4 and δ_C 130.8, 146.0; each *d*), indicating that compound **4** is an oxo-octadecadienoic acid. The pattern of ^{1}H NMR chemical shift values of the four olefinic protons [δ 7.07 (*ddd*, $J=2.8$, 8.8, 15.5 Hz, H-7), 6.03 (*d*, $J=15.5$ Hz, H-6), 6.14 and 6.12 (each 1H, *m*; H-8 and H-9)] were in clear agreement with those reported for a 6*E*,8*E*- diene system of **2**, as well as the analogous *E*,*E*-diene system of alkamides, isolated from *Echinacae spp*. (Bauer et al., 1988). Structure **4** was unambiguously established by detailed 2D NMR spectroscopic studies, including the application of COSY, HMQC and HMBC experiments. The HMBC experiment showed three-bond correlations between $\delta_{C\text{-}5}$ 201.5 and H-7, $\delta_{C\text{-}9}$ 146.0 and H-7, $\delta_{C\text{-}8}$ 130.8 and H-6, and $\delta_{C\text{-}1}$ 179.5 and H-3 (δ 1.57), confirming the placement of carboxylic acid, carbonyl and the two olefinic groups at the C-1, C-5, C-6(7) and C-8(9) positions, respectively. In addition, the HMBC revealed two-bond correlations between $\delta_{C\text{-}5}$ 201.5 and H-4 (δ 2.49), $\delta_{C\text{-}9}$ 146.0 and H-10 (δ 2.13), and $\delta_{C\text{-}1}$ 179.5 and H-2 (δ 2.29), which served to establish structure **4** as 5-oxo-6*E*,8*E*-octadecadienoic acid.

[2] Molecular modeling was done using CS Chem3D Pro Version 5.0 MM2 molecular dynamics minimization followed by MM2 steric minimization. The software was obtained from CambridgeSoft Corporation, 100 Cambridge Park Drive, Cambridge, MA 02140-2312, USA.

This appears to be the first report of compounds **1**–**4** from a natural source. Various hydroxamic acid derivatives were previously isolated, including benzoxazinoids-cyclic hydroxamic acids from the genus *Aphelandra* (Baumeler et al., 2000) and fusarinines A and B from *Fusarium roseum* (Sayer and Emery, 1968), but to our knowledge there is no report regarding hydroxylamino-type derivative, such as 1,2-dihydro-*N*-hydroxypyridines, as natural products. Furthermore, it is intriguing to note that the benzylated derivatives of imidazole alkaloids (including lepidine and lepidine B), analogous to benzylated derivative 1,2-dihydro-*N*-hydroxypyridine (**1**), were previously isolated from *L. sativum* (Bahroun and Damak, 1985; Maier et al., 1998). Finally, several benzylated alkamides (macamides) are currently regarded as chemical markers for 'maca' dietary supplements (Zheng et al., 2000), but to our knowledge macamides **2** and **3** appear to be new markers for *L. meyenii* (maca).

3. Experimental

3.1. General

NMR spectra were acquired on a Bruker Avance DRX-500 instrument at 500 MHz (^{1}H) and 125 MHz (^{13}C), in $CDCl_3$, using the residual solvent signal as int. standard; Multiplicity determinations (DEPT 135°) and 2D NMR spectra (gradient DQF-COSY, HMQC, gradient HMBC and NOESY) were acquired using standard Bruker pulse programs; ^{15}N NMR spectra were recorded at 50.7 MHz using the HMBC pulse program with no low pass filter; chemical shift values are reported relative to liquid NH_3 by calibrating nitromethane to 380.2 ppm; HRMS were obtained by direct injection using a Bruker Bioapex-FTMS with an Analytica Electro-Spray Ionization (ESI) source and the capillary voltage was increased from 80 to 130 to generate collision induced dissociation; TLC: silica gel GF_{254} plates, solvent: CH_2Cl_2:EtOAc (8:2); CC: flash-silica gel G (J.T. Baker, 40 μM Flash); Centrifugal preparative TLC (CPTLC, using Chromatotron®, Harrison Research Inc. Model 8924): 1, 2 or 4 mm Si gel GF Chromatotron™ rotors, (Analtech, Inc.) using a N_2 flow rate of 4 ml min^{-1}. The isolated compounds were visualized by observing under UV-254 nm, followed by spraying with anisaldehyde–H_2SO_4/neutral and acidic aqueous $FeCl_3$/ and Dragendorff's spray reagents.

3.2. Plant material

The tubers of *L. meyenii* were collected in February 1999 from Lima, Peru. A voucher specimen has been deposited at the Herbarium of the University of Mississippi. The material was collected, identified and provided by Frank L. Jaksch Jr.

3.3. Extraction and isolation of compounds

Dried ground tubers of *L. meyenii* (1 kg) were percolated successively at room temperature with petroleum ether (60–80°), $CHCl_3$ and EtOH to yield 138, 21 and 25 g of crude extract, respectively. The dried petroleum ether extract was re-extracted by percolation with $CHCl_3$ (250 ml ×3) that afforded a 16 g $CHCl_3$ soluble fraction. A portion of the $CHCl_3$ fraction (4 g) was subjected to flash-chromatography over Si gel (40 μM, 120 g), using *n*-hexane followed by increasing concentrations of EtOAc (30–70%) in *n*-hexane as eluent, to give four fractions (A–D) after pooling by TLC analysis. Fraction A (110 mg) was subjected to short-flash CC, using 2% EtOAc in CH_2Cl_2 to give **4** (38 mg, R_f 0.68, silica gel, solvent: CH_2Cl_2:EtOAc, 8:2), while fraction B (600 mg) was purified by repeated CPTLC (2mm and 1 mm Si-gel GF disc), using 2% MeOH in CH_2Cl_2 to afford **2** (40 mg, R_f 0.36,), followed by palmitic acid (250 mg) and β-sitosterol (50 mg). Finally, mixture C (80 mg) and D (800 mg) were separately subjected to CPTLC (1 and 4 mm Si-gel GF disc), using 1% MeOH in CH_2Cl_2 and 10% EtOAc in CH_2Cl_2, respectively, to yield **1** (15 mg, R_f 0.56,) and **3** (10 mg, R_f 0.49), respectively.

3.4. Macaridine (3-benzyl-1,2-dihydro-N-hydroxypyridine-4-carbaldehyde) (*1*)

Solid; UV λ_{Max}^{MeOH} (log ε) 208 (4.07), 255 sh (3.76), 294 (4.14) nm; IR ν_{Max}^{film} 3385, *br* (OH), 1658 (CHO), 1494, 1453, 1402, 1372, 1179, 1035, 725, 781 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 9.52 (1H, *s*, H-7), 7.26 (2H, *m*, H-11,13), 7.22 (1H, *m*, H-12), 6.98 (2H, *d*, J=7.1 Hz, H-10,14), 6.94 (1H, *d*, J=4.0 Hz, H-5), 6.29 (1H, *d*, J=4.0 Hz, H-6), 5.73 (2H, *s*, H-8), 4.54 (2H, *s*, H-2); ^{13}C NMR ($CDCl_3$) δ_C 180.2 (*d*, C-7), 142.5 (*s*, C-3), 138.2 (*s*, C-9), 133.2 (*s*, C-4), 129.1 (*d*, C-11,13), 128.0 (*d*, C-12), 126.5 (*d*, C-10,14), 124.8 (*d*, C-5), 111.2 (*d*, C-6), 57.0 (*t*, C-2), 48.9 (*t*, C-8); ESI–HRMS m/z 216.1021 ($[M+H]^+$); (calc. for $[C_{13}H_{13}NO_2+H]^+$, 216.10188).

3.5. N-Benzyl-5-oxo-6E,8E-octadecadienamide (*2*)

Gum, UV λ_{Max}^{MeOH} (log ε) 210 (4.08), 276 (3.99) nm; IR ν_{Max}^{film} 3311 (N-H), 2928, 2845, 1638, 1545, 1239, 1000, 731, 697 cm^{-1}; for ^{1}H NMR spectrum: Table 1; for ^{13}C NMR spectrum: Table 2; ESI–HRMS m/z 384.3034 ($[M+H]^+$); (calc. for $[C_{25}H_{37}NO_2+H]^+$, 384.2903).

3.6. N-Benzylhexadecanamide (*3*)

Solid; UV λ_{Max}^{MeOH} (log ε) 208 (4.03) nm; IR ν_{Max}^{film} 3303 (N-H), 2917, 2849, 1639, 1549, 1454, 730, 696 cm^{-1}; for ^{1}H NMR spectrum: Table 1; for ^{13}C NMR spectrum:

Table 2; ESI–HRMS m/z 346.3142 ($[M+H]^+$); (calc for $[C_{23}H_{39}NO+H]^+$, 346.3104).

3.7. 5-Oxo-6E,8E-octadecadienoic acid (**4**)

Gum; UV λ_{Max}^{MeOH} (log ε) 224 (3.70), 274 (3.49) nm; IR ν_{Max}^{film} 3300–2800 (*br*), 2930, 2857, 1708, 1461, 1410 cm^{-1}; for ^1H NMR spectrum: Table 1; for ^{13}C NMR spectrum: Table 2; ESI–HRMS m/z 295.2319 ($[M+H]^+$); (calc. for $[C_{18}H_{30}O_3+H]^+$, 295.2273).

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Physical–chemical and functional properties of maca root starch (*Lepidium meyenii* Walpers)

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ABSTRACT

The starch of maca (*Lepidium meyenii* Walpers) presented oval and irregular morphology, with granule size between 7.4 and 14.9 μm in length and 5.8 and 9.3 μm in diameter. The isolated starch showed the following features: purity of 87.8%, with 0.28% lipids, 0.2% fibre and 0.12% fixed mineral residue, and no protein detected; the ratio between the amylose and amylopectin contents were 20:80; the solubility at 90 °C was 61.4%, the swelling power was 119.0 g water/g starch and the water absorption capacity was 45.9 g water/g starch; the gel turbidity rose 44% during the storing time; the gelatinization temperature was 47.7 °C and the transition enthalpy 6.22 J/g; the maximum viscosity reached 1260 UB at 46.4 °C, with breakdown, setback and consistence of 850, 440 and −410 UB, respectively. The low gelling temperature and the stability during gel refrigeration could be adequate for foods requiring moderate temperature process, but not for frozen food.

1. Introduction

Maca (*Lepidium meyenii* Walpers) is a native plant in the Andes region and belongs to the *Brassicaceae* family. This root is grown in altitudes varying between 3700 and 4450 m (Vilches, 1998). The maca root is considered a high nutritional value food, similar to that of cereal grains, as it has protein contents between 10% and 18%, carbohydrates between 59% and 76%, as well as a high number of free amino acids and considerable mineral contents, such as Fe, Mn, Cu, Zn, Ca, Na and K, yet with discrete lipid portion, between 0.2% and 2.2% (Dini, Migliuolo, Rastrelli, Saturnino, & Stchettino, 1994; Quiros, Epperson, Hu, & Holle, 1996). The roots are consumed in juices, soups, extracts and processed foods enriched with maca flour, but its availability in pills helped its commercialisation in the international market, especially in Europe and Asia with functional and medicinal claims (Cícero, Bandieri, & Arletti, 2001; Gonzales et al., 2001; Quiros et al., 1996; Vilches, 1998).

Starch is the reserve carbohydrate synthesised by superior plants and constitutes the main source of energy of most living organisms (Núñes-Santiago, Bello-Pérez, & Tecante, 2004). Its presence in roots and tubers such as cassava (*Manihot esculenta*), potato (*Solanum tuberosum*), Peruvian carrot (*Arracacia xanthorrhiza*), as well as in seeds and cereal grains mainly contribute to the texture properties of some foods and as raw material in some industrial applications as thickener, colloidal stabilizer, gelling agent, adhesive and water holding agent (Evans & Haisman, 1997; Godfrey & West, 1996; Lii, Tsai, & Tseng, 1996).

Starch is a polymer composed of about 1 part of amylose and 3 parts of amylopectin. Between 70% and 80% of roots and tubers composition is basically 16–24% starch and 4% lipids and proteins. The size of the granule varies from 1 to 110 μm, depending on the starch source, the granules deriving from tubers being larger than those from cereals (Bemmiller & Whistler, 1996; Hoover, 2001; Núñes-Santiago, Bello-Pérez, & Tecante, 2004; Tester, Karkalas, & Qi, 2004).

Starch degradation *in vitro* owing to amylolytic enzymes varies depending on the starch and the gelatinization grain origin. In the vegetable tissues, the susceptibility to the enzymatic attack is influenced by factors such as the amylose:amylopectin ratio, the crystalline structure, the particle size and the presence of enzymatic inhibitors (Zhang & Oates, 1999).

The starches major physical–chemical and functional properties for feeding ends and other industrial applications are gelatinization, retrogradation, solubility, water absorption power, syneresis and their rheological behaviour in pastes and gels. These physical–chemical and functional properties are influenced by the shape, molecular structure and botanical source of native starches in the different vegetable sources (Svegmark & Hermansson, 1993; Wang & White, 1994).

In the present study, the aim was to investigate some physical–chemical and functional properties of the starch extracted from maca (*L. meyenii* Walpers) roots as parameters of potential use in food products. Comparatively, more widely known starches such

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as cassava and Peruvian carrot were employed, both also native from the central and Andean regions of South America.

2. Materials and methods

2.1. Materials and reagents

The maca roots (*L. meyenii* Walpers) were acquired in the State of Arequipa, Peru, 4 days after-harvest; they were washed in 1% sodium hypochlorite solution and dried at ambient temperature. After cleaning, the roots were stored in polyethylene bags and frozen at −18 °C until their use.

All the reagents employed were purchased either from Sigma Chemical Co., or Aldrich Chemical Co.

2.2. Starch extraction

The starch from maca roots was extracted using a slight modification of the method described by Singh and Singh (2001). Roots were manually peeled, cut into small cubes (approx. 3 cm^3) and were ground with water in a blender for 5 min. The homogenate was filtered through muslin cloth. The residue left on the muslin cloth was washed with distilled water. Filtrate was collected in a glass beaker and the residue in the muslin cloth was discarded. The supernatant liquid was decanted, the starch layer was reslurried in distilled water and, again, starch was allowed to settle. This was repeated for 8–10 times until the supernatant became transparent. The starch cake was collected and dried at a temperature of 40 °C in a hot air cabinet drier.

2.3. Physical–chemical properties of starch

2.3.1. Scanning electron micrographs

The size and shape of the starch granule were observed by means of a backscattering electron microscope model Joel JSM 840 (IF-USP). Starch samples were coated with gold by the "sputtering" process, by an Edwards Sputter Coater 150B metalizer. The granules measurement was reported as the averages of the diameters and lengths taken from 30 granules per field.

2.3.2. Determination of the chemical composition

The chemical composition was determined in the roots and in the starch extracted from maca, following the AOAC (1990) and local norms (Instituto Adolfo Lutz., 1985); the total starch analysed by the method described by Areas and Lajolo (1981) and the total carbohydrates were estimated by difference. The dietary fibre (DF) content was determined by the enzymatic–gravimetric method (Prosky, Asp, Schweizer, Devries, & Fuerda, 1992). The total sugars were measured by the phenol–sulfuric reaction (Dubois, Gilles, Hamilton, Rebers, & Smith, 1959) and the reducing sugars by the 3,5-dinitrosalicylic acid reagent (DNS) described by Bernfeld (1951).

2.3.3. Amylose content (%)

The starch amylose content extracted was determined following the Morrison and Laignelet method (1983) with some modifications. A volume of 5.0 ml of UDMSO (dimethyldisulfide and urea at 6 M, 9:1) were added to a 40 mg isolated starch sample; the suspension was vigorously shaken and incubated in a boiling bath for 30 min, placed in a stove at 100 °C for 90 min. A 0.5 ml aliquot of this solution was diluted to 50 ml with distilled water and 1.0 ml I_2–KI (2 mg I_2, 20 mg KI/ml). Finally, the absorbance at 635 nm was measured in a UV–Vis B582 spectrophotometer. The amylose content was determined from a standard curve, using amylose and amylopectin solutions.

2.3.4. Swelling power (SP), water absorption capacity (WAC) and solubility

The maca starch granules swelling power and solubility were triply determined following the method proposed by Leach, McCowen, and Schoch (1959). Aqueous suspensions of 2% starch (w/v) were heated in a water bath at constant temperatures and shaking, for 30 min. Each suspension was cooled and centrifuged at 3000*g* for 15 min; the decanted was weighed and the supernatant was placed in a vacuum stove at 120 °C for 4 h. The data obtained were used to calculate the water absorption capacity, the swelling power and the solubility of the starch granules.

2.3.5. Turbidity

The maca starch gels turbidity was measured as described by Perera and Hoover (1999), by means of a 1% aqueous suspension placed in water bath at constant temperature (90 °C) and constantly shaken for 1 h. The paste was cooled at ambient temperature and stored at 4 °C for 5 days; turbidity was measured at every 24 h, measuring the absorbance at 640 nm in a spectrophotometer (Micronal B582) from time zero.

2.3.6. Stability to freezing and refrigeration

The conditions established for determining stability to freezing and refrigeration were adapted from Eliasson and Ryang (1992). A starch suspension at 6% was heated up to 95 °C for 15 min; it was next cooled to 50 °C and kept at this temperature for 15 min. Aliquots of 50 ml were placed in centrifuge tubes and these were conditioned at three temperatures: ambient, 4 °C and −10 °C, for 5 days. After every 24 h, the samples were centrifuged at 8000*g* for 10 min and later the amount of water expelled during storage was measured.

2.4. Thermal properties

2.4.1. Starch paste properties

The maca starch paste properties were determined according to the method described by Wiesenborn, Orr, Casper, and Tacke (1994), using a viscoamylograph (Brabender PT-100. Germany). An aqueous suspension of 8% starch (dry basis) was heated from 25 to 95 °C at a 1.5 °C/min range and kept at 95 °C for 20 min, and later cooled up to 50 °C at the same temperature range and kept at this second temperature for 20 min. The results obtained from the amylogram were used to calculate the maximum viscosity, consistence, breakdown and setback in Brabender Units (BU).

2.4.2. Differential scanning calorimetry (DSC)

For determining the starch gelatinization temperature, a DSC was employed, (model 822^e, Mettler Toledo, Simple Robot, TSO 801R0, operated by EXSTAR6000 Software), using the technique described by Ruales and Nair (1994), somewhat adapted. To 3.0 mg starch samples (dry basis) 70% distilled water were added to form a suspension. The capsule was hermetically sealed and balanced at ambient temperature for 1 h before being heated in the equipment. The calibration of the system was conducted with metallic indium and an empty aluminum capsule taken as reference. The samples were analysed between 10 and 120 °C at a heating range of 10 °C/min. The starch samples thermal transitions were defined as T_o (initial temperature), T_p (peak temperature), T_f (final temperature) and ΔH_{gel} concerning the gelatinization enthalpy. The enthalpies were automatically calculated from the starch samples on a dry mass basis.

2.4.3. Texture properties of the starch gel

The maca starch gel texture properties were determined from the texture analysis profile (TAP) using a TA/XT2 equipment (Stable Microsystems, Surrey, England). A starch suspension at 6%

was heated up to 95 °C for 15 min, later cooled to 50 °C and kept at this temperature for 15 min. The paste formed was transferred in 40 ml portions in 50 ml beaker flasks and cooled at ambient temperature; they were later stored at 4 °C for 24 h. The gels formed in the flasks were directly used in the texture analysis, and each gel was penetrated 10 mm by a cylindrical probe of P/25 diameter. Two strength–time curves were obtained with 1.0 mm/s speed, during the penetration cycles. From the texture profile curve, fracturability, hardness, cohesiveness, adhesiveness, springiness, gumminess and chewiness were calculated. The TPA analyses were triply conducted.

3. Results and discussion

3.1. Granule size by scanning electron micrographs

The maca starch granule morphology and distribution are shown in Fig. 1. The maca starch granules presented oval and irregular morphology with a distribution between 7.4 and 14.9 μm in length and 5.8 and 9.3 μm in diameter. The morphology observed was similar to that of biri (*Canna edulis*) and oca (*Oxalis tuberosa*) starch, also known as Andean roots, with sizes between 35 and 101 μm, and 22 and 55 μm, respectively (Santacruz, Koch, Svensson, Ruales, & Eliasson, 2002).

Some authors have demonstrated the influence of the temperature variation in the cultivation of sweet potato, wheat and maize, concerning the starch granule size and have observed the decrease in size and, consequently, changes in the starch granules physical–chemical properties (Lu, Jane, Keeling, & Singletary, 1996; Noda, Kobayas, & Suda, 2001; Singh, Seib, & Bernardin, 1994). As to maca starch, probably the environmental conditions (temperatures from 4 to 7 and −10 °C) for cultivating the root could influence the starch granule morphology and size. Yet, there are neither records of the cultivation of this product in other environmental conditions, nor studies concerning the maca starch properties, which does not allow for confirmation of this hypothesis.

Table 1
Chemical composition of maca root and starch

Components	(%) Dry basis	
	Maca root	Maca starch
Crude protein	17.69 ± 1.96	NI*
Lipids	3.61 ± 0.04	0.28 ± 0.03
Carbohydrates	72.78 ± 0.2*	99.06 ± 0.02*
Fibre soluble	8.50 ± 0.32	NI*
Fibre insoluble	23.24 ± 0.07	0.2 ± 0.01
Total starch	23.17 ± 1.06	87.83 ± 0.87
Total sugar	18.87 ± 0.35	1.53 ± 0.52
Sugar reducing	13.10 ± 0.17	1.21 ± 0.65
Amylose	ND*	20.45 ± 0.91
Amylopectin	ND*	79.54 ± 0.91
Ash	5.93 ± 0.18	0.12 ± 0.01

ND*, not determined; NI*, not identify.
* Determined for difference.

3.2. Chemical composition

The results referring to the maca starch chemical composition are shown in Table 1. The isolated starch presented 0.28% lipids, 0.2% fibre and 0.12% fixed mineral residue, but it was not possible to quantify the protein content because of its low content. The isolated starch purity was 88%, which represents high purity when compared to the purity of some *Pachyrhizus ahipa* varieties (56–59%) and those similar to the red sweet potato (87%) (Osundahunsi, Fagbemi, Kesselman, & Simón, 2003; Torruco-Uco & Betancur-Ancona, 2007).

The maca starch presented 20.5% amylose and 79.5% amylopectin (Table 1), this result differs for maize starches (28.3% and 71.7%), red sweet potato (34.2% and 65.8%), malanga (*Xanthosoma saggitifolium*) (24% and 76%) and makal (*Xanthosoma yucatanensis*) (22.4% and 77.6%) (Charles, Chang, Ko, Shiroth, & Huang, 2005; Moorthy, 2002; Osundahunsi et al., 2003; Torruco-Uco & Betancur-Ancona, 2007).

In different cultivations of sweet potato, the starch content varies from 43% to 79% and in it the amylose content goes from 17% to 22% (Madhusudhan, Susheelemma, & Tharanathan, 1992). This can be influenced by the botanical source, the climatic conditions and

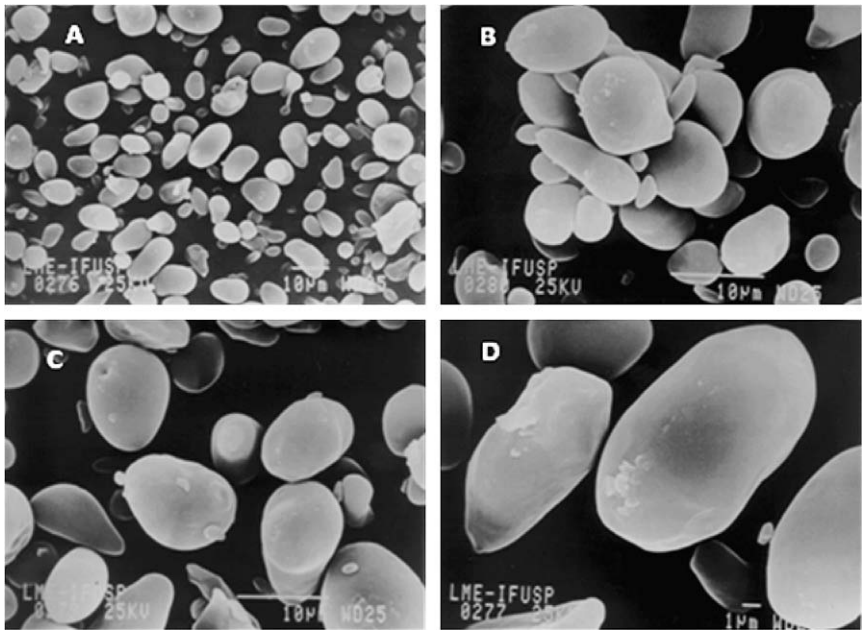

Fig. 1. Scanning electron micrographs (SEM) of maca starch. A: (×550, bar = 10 μm); B: (×1400, bar = 10 μm); C: (×1500, bar = 10 μm); D: (×3000, bar = 1 μm).

types of soil during cultivation, as well as the harvest time, being that a late potato harvest may reduce it from 22% to 18% (Noda et al., 2004).

3.3. Swelling power (SP), water absorption capacity (WAC) and solubility

The swelling power (SP), the water absorption capacity (WAC) and the solubility of maca starch are directly correlated to the increment in temperature. Fig. 2A, B (SP), and C (WAC) show the swelling power, the water absorption capacity and the solubility of the maca starch granules, respectively. As can be seen from the figures, low levels of SP were verified; WAC and solubility at temperatures of 30 and 40 °C can be observed, with gradual swelling of the granule from 50 to 90 °C. The swelling power of the maca starch granules at 90 °C was 119.0 g water/g starch, the water absorption capacity was 45.9 g water/g starch and 61.4% solubility; these data are high if compared to the cassava starch (Fig. 2B), or with the data observed by Betancur-Ancona, Chel-Guerrero, Camelo Matos, and Davila-Ortiz (2001), which was 58.8 g water/g starch. Equally high are the values of some maize varieties (13.7–20.7 g water/g starch) (Sandhu & Singh, 2007) and different potato varieties (36.5–40.5 g/g) (Singh, McCarthy, & Singh, 2006).

Starches such as amylose in reduced proportion show high swelling power and low solubility when heated in excess water. The crystalline molecular structure of starch is broken and the water molecules are bonded to the free hydroxyl groups of amylose and amylopectin by hydrogen bonds, which could cause an increment in the absorption capacity and solubility (Singh, Singh, Kaur, Sodhi, & Gill, 2003).

3.4. Turbidity

The gelatinized maca starch suspensions presented relative stability during storage, showing a small reduction in absorbance after the first day (from 0.51 to 0.49 nm) with a small increase after the second storing day (Fig. 3). It can also be observed in the figure that maca starch is more stable than Peruvian carrot starch and similar to cassava starch (Fig. 3). In potato starches, turbidity gradually increased in the first 5 days of storage at 4 °C, varying from 1.25 to 1.85 nm from the 1st to the 5th storing day (Kauar, Singh, & Sodhi, 2002). Sandhu and Singh (2007) observed a progressive increase in gel turbidity from 1.6 to 2.2 nm in maize varieties, during storage between 0 and 120 h.

3.5. Stability to freezing and refrigeration

Syneresis characterises the starch stability to freezing and refrigeration as shown in Fig. 4. The paste presented high stability when stored at ambient temperature and under refrigeration (4 °C), not presenting syneresis. However, the paste showed low stability to freezing in the storing period (−10 °C) and, therefore, high syneresis (4.5%) when compared to cassava and Peruvian carrot starch (Fig. 4). Starches with high amylose value influence the gelatinization and retrograding properties. Starches with high amylose content such as potato (20.1–31.0%), maize (22.4–32.5%), taro (28.7–29.9%) and cassava (18.6–23.6%) present high syneresis, due to the large amount of water expelled during the retrograding process (Gunaratne & Hoover, 2002; Singh et al., 2003). The low syneresis in starch pastes is attributed to the low amylose content, and also to the possible aggregation and to the amylose crystallization occurring during the first storing hours, whilst in amylopectin it would occur at later stages (Miles, Morris, Oxford, & Ring, 1985; Singh et al., 2006).

The paste retrogradation is indirectly influenced by the structural arrangement of the starch chains within the amorphous and crystalline regions of the non-gelatinized granule, acting in the granule breakdown during gelatinization and also in the interactions occurring within the starch chains during the gel storage (Perera & Hoover, 1999).

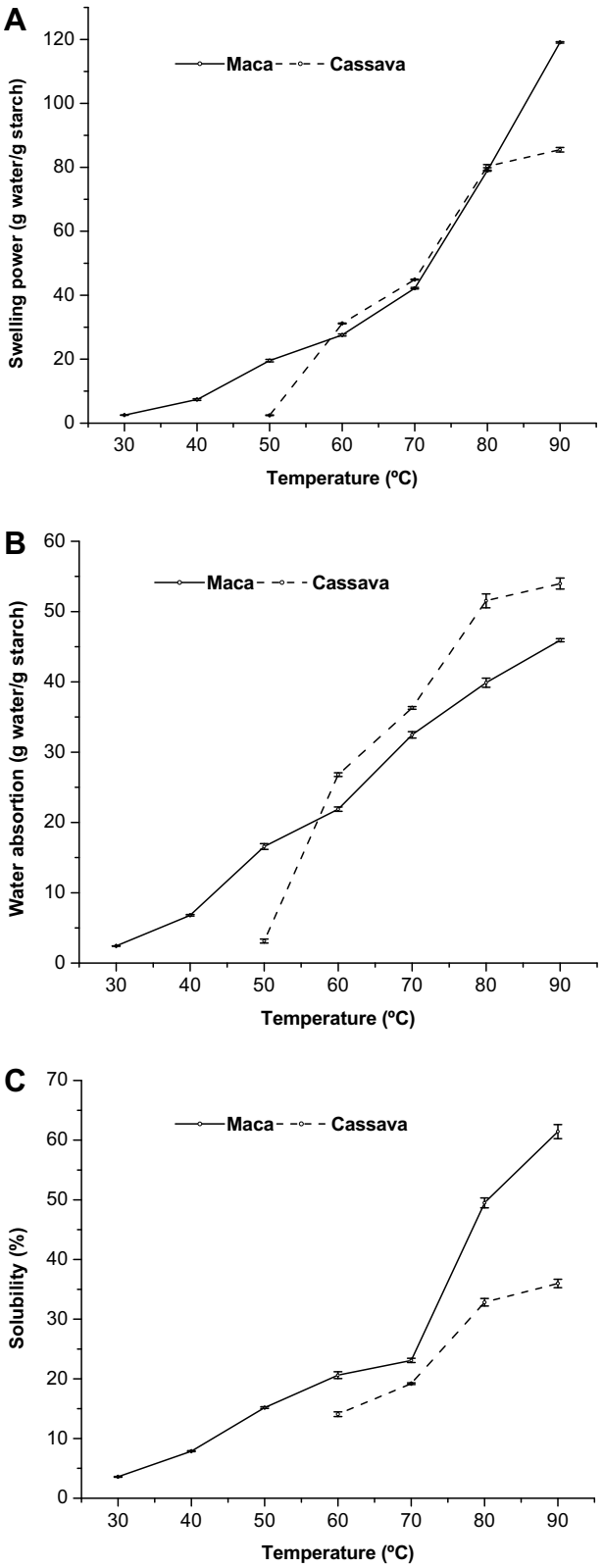

Fig. 2. Comparative hydration curves of starches of maca and cassava as a function of the temperature. A: Swelling power; B: Water absorption capacity; C: Solubility (%).

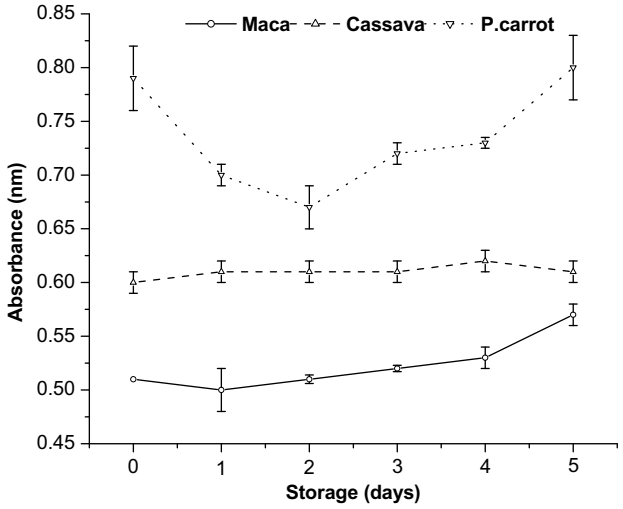

Fig. 3. Effect of storage time on the turbidity starch compared with other starches.

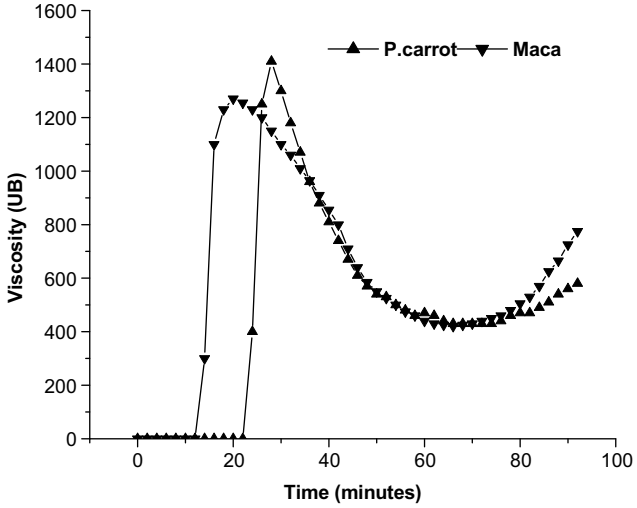

Fig. 5. Viscoamylogram of maca and Peruvian carrot starches.

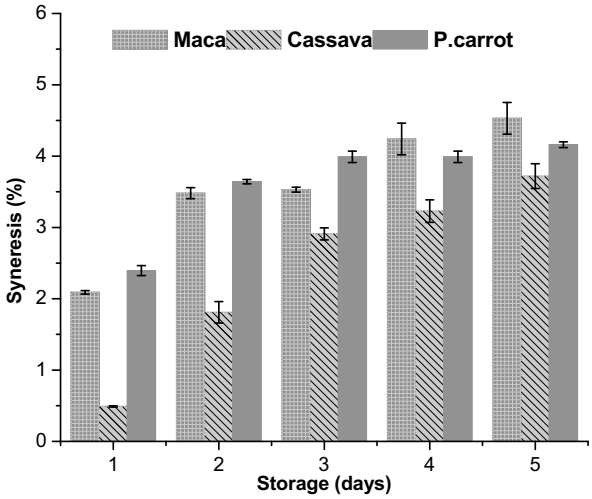

Fig. 4. Refrigeration stabilities of maca starch compared with cassava and Peruvian carrot starches.

Table 2
Paste properties of maca and Peruvian carrot starches

Parameters	Starch	
	Maca	P. carrot
Peak viscosity (BU)	1260	1400
Viscosity at 95 °C (BU)	780	610
Peak viscosity temperature (°C)	46.4	62
Viscosity at 95 °C for 20 min (BU)	410	470
Viscosity at 50 °C (BU)	850	580
Breakdown (BU)[a]	850	930
Consistency (BU)[b]	−410	−820
Setback (BU)[c]	440	110

BU, Brabender units.
[a] Breakdown: peak viscosity (BU) – viscosity at 95 °C for 20 min (BU).
[b] Consistency: viscosity at 50 °C (BU) – peak viscosity (BU).
[c] Setback: viscosity at 50 °C (BU) – viscosity at 95 °C for 20 min (BU).

3.6. Thermal properties

3.6.1. Paste properties

The paste properties are influenced by several factors, such as granule size, the amylose/amylopectin ratio, molecular characteristics of the starch and the conditions of the thermal process employed to induce gelatinization (Zhou, Robards, Glennie-Holmes, & Helliwell, 1998).

Fig. 5 and Table 2 show the rheological behaviour of maca starch and Peruvian carrot starch measured in the Brabender Viscoamilograph. The figure shows that the maca starch profile presents similarities to that of Peruvian carrot (Fig. 5). During the heating from 25 to 95 °C (for 40 min) the maca starch paste presented a maximum viscosity peak of 1260 Brabender Units (BU) after 20 min of heating; at this peak, the temperature was 46 °C. Considering the maca starch gelatinization temperature, at 95 °C it presented 780 BU, and after 20 min at the same temperature, the viscosity fell to 410 BU, rising to 850 BU at the end of the cooling cycle, at 50 °C. The breakdown value of the maca starch paste is high (850 BU) when compared to that of makal (−8 BU), cassava (306 BU) and maize (22 BU) starches (Torruco-Uco & Betancur-Ancona, 2007), but is lower than that of Peruvian carrot (930 BU). The consistency of the maca starch paste presents a negative value (−410 BU), a very low value as compared to makal, cassava and maize (180 and 282 BU, respectively) (Betancur-Ancona et al., 2001; Torruco-Uco & Betancur-Ancona, 2007) and Peruvian carrot (−820 BU). The setback value was 440 BU, which is considered high in the case of cassava, makal and maize (−231, 172 and 304 BU, respectively) (Betancur-Ancona et al., 2001). Low consistence and setback values increase stability paste in mechanical processes and reduce the tendency in retrograding during cooling, this being the case of starches with high swelling power and consequently high viscosity, such as the potato, cassava and waxy starches (Osundahunsi et al., 2003). The granules of these starches markedly swell when cooked in water and the forces turn fragile due to the mechanical shaking, resulting in instability during cooking (Sandhu & Singh, 2007). Conversely, starches rich in amylose present granules with limited swelling due to the internal stiffness of strongly associated linear molecules, and the granules of these starches do not swell enough to form viscous pastes when cooked in water under normal conditions (Sandhu & Singh, 2007).

3.6.2. Diferencial scanning calorimetry (DSC)

The maca starch gelatinization temperature presented a low value, with a 45.7 °C initial temperature (T_o), the gelatinization peak temperature (T_p) was 47.7 °C, the final temperature (T_c) was 51.16 °C, and the gelatinization enthalpy (ΔH_{gel}) was 6.22 J/g, results shown in Table 3 and Fig. 6.

Table 3
Gelatinization properties of cassava, maca and Peruvian carrot starches

Variety	T_o (°C)	T_p (°C)	T_c (°C)	ΔH_{gel} (J/g)
Cassava	61.54	64.82	69.45	9.85
Maca	45.7	47.7	51.16	6.22
Peruvian carrot	59.54	61.95	65.86	10.48

T_o, onset temperature; T_p, peak temperature; T_c, final temperature; ΔH_{gel}, enthalpy gelatinization.

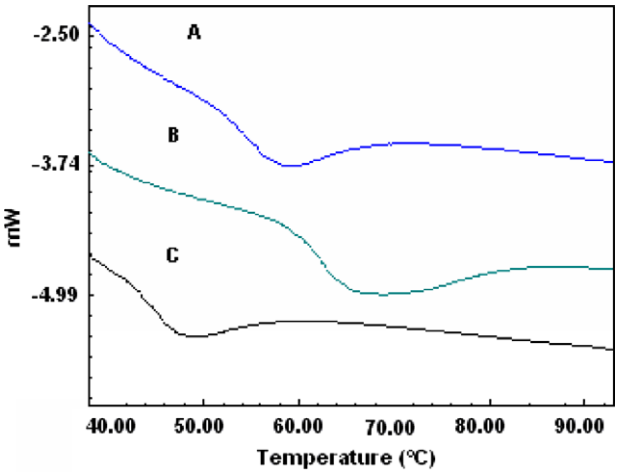

Fig. 6. DSC endotherm curves of gelatinization of starches from different: (A) Peruvian carrot; (B) cassava; (C) maca.

The gelatinization temperature of maca starch was lower as compared to the gelatinization temperatures of cassava (61.5, 64.8 and 69.4 °C) and Peruvian carrot starches (59.5, 61.9 and 65.8 °C), employed as reference for comparing data (Table 3) In the literature, gelatinization temperature data can be found for different products, such as: maize (62.4, 66.3 and 72.9 °C) (Betancur-Ancona et al., 2001), white sweet potato (66.7, 70.7 and 74.8 °C), potato (60, 69 and 80 °C) and cassava (6.4, 69.3 and 84.1 °C) (Osundahunsi et al., 2003; Pérez, Breene, & Bahnassey, 1998). In maca starch, low gelatinization temperature indicates that the beginning of gelatinization requires less energy (ΔH_{gel} = 6.22 J/g) as compared to the Peruvian carrot and cassava starches (10.5 and 9.8 J/g), respectively, and the ones shown by Betancur-Ancona et al. (2001) for cassava (9.6 J/g) and maize (10.3 J/g), as well as for white sweet potato (10.5 J/g) (Osundahunsi et al., 2003).

Li, Berke, and Glover (1994) reported ΔH_{gel} in the 8.2 to 12.3 J/g range for different tropical maize starches, and explained that the variation of gelatinization energy could present differences amongst the bonding forces of the double helix forming the amylopectin crystallography, which resulted in different alignments of the hydrogen bonds within the starch molecules (Sandhu & Singh, 2007).

3.6.3. Texture properties of starch gel

The texture properties of maca gel and of the starches employed as reference (cassava and Peruvian carrot) were determined by a texture analyser and are shown in Table 4 and Fig. 7. The profile of the maca starch gel texture presented high fracturability (2.2 N) and hardness (4.1 N) and lower values of adhesiveness and cohesiveness when compared with cassava and Peruvian carrot starches (Table 4). The gel firmness is mainly caused by the starch gel retrograding, which is associated with the syneresis of water and amylopectin crystallization loss, starches with high paste viscosity result in gels with high stiffness and cracking (Miles et al., 1985). Starch gels presenting high stiffness tend to have high amylose content and long amylopectin chains (Mua & Jackson, 1997). In a potato starch variety, Singh and collaborators (2006) found high fracturability and hardness, attributing this property to the presence of a high percentile of wide granules and low amylose content.

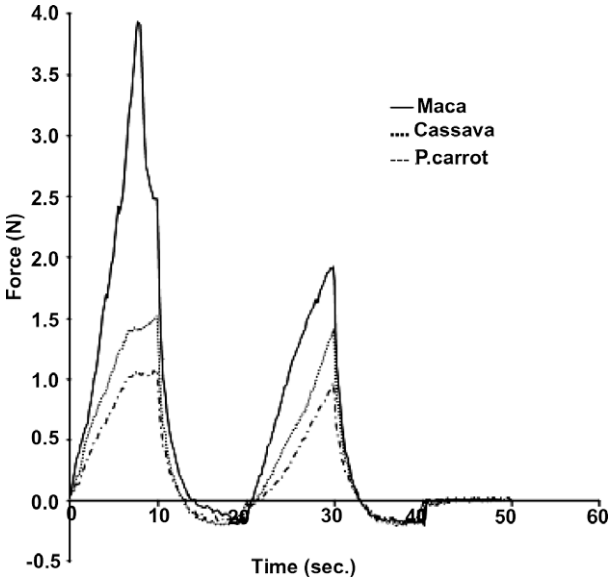

Fig. 7. Texture profile analysis (TPA) curves of starch gels from: (A) maca; (B) cassava; (C) P. carrot.

4. Conclusions

The physical–chemical and functional properties of maca starch (*L. meyenii* Walpers), a non-conventional source, suggest that this product may serve as a model ingredient for foods and other industrial applications that require processing at low temperatures and dispense freezing. The maca starch granules presented different sizes with granules between 7.4 and 14.9 μm in length and 5.8 and 9.3 μm in diameter, which are considered small. For the low amount of protein, the isolated starch could have a wide use for making high-glucose syrup. The 47.6 °C gelatinization temperature of this starch, together with a water absorption capacity of 45.9 g of water/g, swelling power of 119.0 g water/g and 61.4% solubility at 90 °C are of great importance in products subjected to low temperatures during processing. However, the high firmness and stability of the gel during refrigeration could be adequate as thickener, stabilizer and jellifying agent in refrigerated foods,

Table 4
Textural properties of starch gels from maca, Peruvian carrot and cassava

Starch	Fracturability (N)	Hardness (N)	Adhesiveness (Ns)	Cohesiveness	Gumminess (N)	Springiness (s)	Chewiness (Ns)
Maca	2.231	4.126	0.7925	0.506	2.085	0.912	1.901
P. carrot	1.760	0.879	1.986	0.582	0.947	0.850	0.805
Cassava	1.077	1.096	0.910	1.037	0.627	0.815	0.511

despite being inadequate in frozen foods due to the syneresis after retrograding. These values may credit maca as a source for new forms of starch for special purposes, although the low production of the plant for industrial ends is acknowledged.

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