

## Dansk resume om soja til menneskelig indtagelse

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### Forord

Formålet med denne litteraturgennemgang er at levere et kritisk sammendrag af den eksisterende videnskabelige viden om sojas forskellige egenskaber og potentielle sundhedsfremmende- og skadelige effekter. Mange dele af sammendraget handler om soja og soja produkter i det hele taget, men der lægges speciel vægt på forarbejdede soja produkter og i særdeleshed på teksturerede sojaproteiner, såsom produkterne fra Soy4you.

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## 1. Introduktion

*Soja produkter vinder i stadig større grad indpas på danskernes spiseborde, og kan på længere sigt blive en sund erstatning for mange andre proteinkilder.*

Sojabønner (*Glycine max*) er en bælgplanten, som naturligt findes i Østasien, hvor den i årtusinder har været dyrket og har leveret olie og protein. Sojabønner dyrkes nu i store dele af verden, og er den fjerde største afgrøde, kun overgået af hvede, ris og majs. Planten har gennemgået en lang kæde af forædlingsarbejde for at fremme sammensætningen af bønnerne og dens dyrkningsmæssige kvaliteter. Mængden af fedtreducerede proteiner som det nu til dags lader sig gøre at producere fra sojabønner gør det muligt at opdrætte kødproducerende dyr på en hidtil uset skala i menneskehedens historie. Kun en ganske lille andel af afgrøden indtages indtil videre direkte af mennesker.

I Østasien har man gennem årtusinder spist soja tilberedt på mange forskellige måder. De mest almindelige inkluderer bl.a. gærede sojaprodukter, sojamælk og tofu. Nu til dags har den teknologiske udvikling gjort det muligt at raffinere de enkelte bestanddele af sojabønner og fjerne uønskede elementer. Soy4you® og Soy4you øko® er resultatet af en sådan højteknologisk og kompleks raffinering, således at man ender med et produkt, der indeholder præcis de elementer fra sojabønner som er ønskelige og samtidig får et produkt, der møder forbrugernes ønske om at det i struktur minder om hakket kød.

*Soy4you® og Soy4you øko® giver et sundt og ernæringsrigtigt alternativ til andre proteinkilder*

## 2. Indholdet i sojabønner

*Sojabønner har et forholdsvis lavt indhold af fedt og kulhydrater og et højt indhold af proteiner, og indeholder derudover en række helbredsgavnige elementer*

Der er forsket meget i sojabønner, og derfra ved man rigtig meget om hvad sojabønner består af, og hvorfor den har så mange sundhedsfordele. Sojabønner er en rigtig god kilde til protein og fibre og indeholder gode mængder af molybdenum, jern, calcium og fosfor samt B1-vitamin, B2-vitamin, B6-vitamin, E-vitamin og folinsyre. Derudover er soja bl.a. en kilde til sundhedsfremmende antioxidanter, isoflavoner og flerumættede fedtsyrer.

*Proteiner* Rå sojabønner indeholder ca. 40% proteiner, primært de såkaldte lager proteiner glycinin and beta-conglycinin, men indeholder også biologisk og metabolisk aktive proteiner såsom enzymer, trypsinhæmmere, proteaser og hemagglutininer. Lager proteinerne udgør 60-70% af bønnernes protein, og er samlede som partikler, såkaldte ”protein legemer”, som opbevares i bønnerne indtil spiringen begynder, hvorefter de gradvist nedbrydes til aminosyrer og transporteres til bønnens vækstpunkt. Protein legemernes kompakte natur gør det vanskeligt for den menneskelige krop at fordøje lagerproteinerne og optage aminosyrerne derfra. Varme- og trykbehandling af soja ændrer lagerproteinernes struktur, og gør det nemmere at fordøje dem.

*Kulhydrater* Sojabønner har et relativt lavt indhold af kulhydrater (35%) og næsten alle kulhydraterne i soja er oligosaccharider eller ufordøjelige fibre. De primære opløselige sukkerstoffer er det fordøjelige sukrose og det ufordøjelige raffinose og stachyose, som kan bidrage til tarmgas og mavebesvær. Fibrene består primært af cellulose, hemicellulose og pektin.

*Olier og fedt* Rå sojabønner indeholder ca. 20% fedt, og har dermed et relativt højt fedtindhold. De primære umættede fedtsyrer er de flerumættede  $\alpha$ -linolsyre (Omega-3)(7-10%), og linolsyre (Omega-6)(50-60%); og den enkeltumættede oleinsyre (20-25%). Soja indeholder desuden de mættede fedtsyrer stearinsyre (3-7%) and palmitinsyre (5-10%).

*Phytoøstrogener* Sojabønner indeholder en række forskellige isoflavoner og coumestaner, som samlet set kaldes for phytoøstrogener (planteøstrogener). Phytoøstrogener er molekyler der har den egenskab at de enten direkte eller indirekte kan påvirke reguleringen eller virkningen af menneskelige kønshormoner i kroppen. Ved den direkte påvirkning ligner phytoøstrogenmolekylerne rigtige hormoner så meget at de kan passe ind i de ”nøglehuller”, som det ellers kun er kønshormonerne der passer ind i. Ved en indirekte påvirkning kan phytoøstrogenerne påvirke om der dannes og udskilles mere eller mindre af kroppens egne kønshormoner. Isoflavonerne er dem der har tiltrukket sig den største opmærksomhed, da de sættes i forbindelse med de mest markante gavnlige helbredsvirkninger hos mennesker.

*Antifordøjelige elementer* Rå sojabønner indeholder en række elementer der har uønskede effekter på fordøjelsen eller fødeoptagelsen i den menneskelige tarm. *Phytansyre* har gavnlige antioxidative egenskaber, men har desuden en kraftig evne til at binde sig til mineraler såsom jern, zink og kalk, således at disse ikke kan optages i kroppen. Varmebehandling af sojaprodukter reducerer phytansyrens virkning kraftigt. Derudover findes der i rå bønner *trypsin hæmmere*, som modvirker at kroppens enzymer kan nedbryde proteiner i tarmen. Trypsin hæmmerne kan slås i stykker ved varmebehandling og mister derved deres uønskede virkning. *Lektiner* er en naturlig del af mange bønner og er giftige for mennesker i større mængder. De binder sig til tarmvæggen og forhindrer tarmcellerne i at udvikle sig normalt, således at fødeoptagelsen hæmmes. Lektinerne nedbrydes ved varmebehandling.

*Fibre* De forholdsvis store mængder af uopløselige fibre i sojabønner virker rigtig godt på fordøjelsen og reducerer kolesterol i blodet og hæver tolerancen overfor sukker og gør cellerne mere reaktive på insulin. Det betyder at sojabønner også er godt i tilfælde af forstoppelse, diarré, for højt kolesterol og diabetes.

*Soy4you® og Soy4you øko® er forarbejdede produkter, som på væsentlige punkter adskiller sig fra de rå sojabønner*

### 3. Indholdet i Soy4you® og Soy4you øko® i forhold til rå sojabønner

*Soy4you® og Soy4you øko® er forarbejdet på sådan måde at produkterne giver en bedre nedbrydelighed af proteinerne og mindsker eller fjerner flere uønskede elementer i forhold til andre soja produkter*

Når man taler om soja, skal man være opmærksom på, at soja ikke bare er soja, men at indholdet og egenskaberne af det enkelte sojaprodukt afhænger meget af den behandling sojabønnen har oplevet fra den høstes til den spises. Man kan groft dele de mest gængse sojaprodukter op i 3 kategorier: uforarbejdede, fermenterede og forarbejdede sojaprodukter.

Soy4you® og Soy4you øko® er begge forarbejdede produkter, som kaldes for fedtreducerede teksturerede protein isolater, idet størstedelen af olie/fedt-elementerne er fjernet, således at primært protein-, og kulhydrat- og fiberbestanddelene er tilbage. Proteinandelen i produkterne ligger typisk på ca. 50%. Processerne, hvorved Soy4you® og Soy4you øko® produkterne frembringes er en smule forskellige, idet fedt/oliedelen i Soy4you® fjernes ved en vaskeproces med alkohol, mens den i Soy4you øko® fjernes ved en koldpresning. Derudover gennemgår begge produkter en række af forskellige varme-, tørrings- og trykprocesser, der hver især har indvirkning på produkternes indholdsstoffer og deres fordøjelses- og optagelsespotentialer i menneskekroppen.

I forhold til de rå sojabønner gør fremstillingen at Soy4you® og Soy4you øko® -

1. Har et væsentligt lavere indhold af fedtstoffer.
2. Har en ændret protein sammensætning, der gør det nemmere for kroppen at nedbryde og optage aminosyrerne.
3. Har et væsentligt lavere indhold af trypsin hæmmere, som ellers kan have en forstyrrende effekt på nedbrydningen af proteiner i tarmen.
4. Har et væsentligt lavere indhold af potentielt allergifremkaldende proteiner.
5. Har et lavere indhold af isoflavoner (Specielt Soy4you®, mens en større del er bevaret i Soy4you øko® )
6. Har en lavere antioxidant effekt.

*I fremstillingen af Soy4you® og Soy4you øko® er der i højere grad fokuseret på den ernæringsmæssige værdi end på de medicinske effekter*

#### 4. Det komplette protein

*Isolerede soja proteiner er et af de få planteproteiner, der indeholder alle de aminosyrer som kroppen har brug for i tilstrækkelige mængder, og kaldes derfor et komplet protein*

Det er vigtigt at forstå at proteiner ikke bare er proteiner, men er komplekse molekyler som indbyrdes kan have store forskelle i bl.a. - hvilke aminosyrer de indeholder, - hvor vandopløselige de er, - hvor syrereaktive de er, - hvor let de nedbrydes i kroppen, - og hvor let de optages i kroppen. Proteiner findes i mange planteprodukter, men ikke alle planteproteiner indeholder alle de essentielle aminosyrer (eller ikke i tilstrækkeligt tilgængelige mængder) til at menneskekroppen kan opretholde en naturlig metabolisme. Man taler derfor om ”Det Komplette Protein”, hvis en proteinkilde leverer alle de bestanddele, som menneskekroppen har brug for.

Hvis man ønsker helt eller delvist at lade planteproteiner være kilden til det daglige proteinindtag, er det meget vigtigt at man har en forståelse for sammensætningen, kvaliteten og udnyttelsesgraden af proteiner fra forskellige kilder. Til det formål har man udviklet metoden PDCAAS (Protein Digestibility Corrected Amino Acid Score), som de amerikanske sundhedsmyndigheders (FDA) og FN's fødevarer- og sundhedsorganisationer (FAO og WHO) anerkender som den bedste egnede metode til at vurdere hvorvidt en proteinkilde leverer ”Det Komplette Protein”. I PDCAAS analysen sammenholder man den undersøgte proteinkilde med en kendt proteinkilde, og vurderer hvorvidt aminosyreprofilen lever op til kravet om indhold af essentielle aminosyrer og kvælstof (nitrogen) hos et 2-5 år gammelt barn, da dette anses for at være det tidspunkt i et menneskes liv, hvor behovet for ”Det Komplette Protein” er størst. Herefter korrigeres der for den faktiske fordøjelighed af proteinet ved analyse af, hvor stor en del af proteinet der genfindes i fæces hos forsøgsrotter. PDCAAS metoden giver en score fra 0 til 1, hvor 1 angiver at proteinet er et ”Komplet Protein”, mens f.eks. scoren 0,7 angiver at proteinet ikke lever op til kravene om at levere de elementer som en menneskekrop har behov for i de rette mængder.

Soja protein isolat er en af de få planteproteinkilder, der indeholder det Komplette Protein (PDCAAS = 1.00) (30), og ligger derved på linje med æggehvide, kasein- og valleprotein (mælkeproteiner), og oksekød (alle med PDCAAS = 1.00), hvorimod f.eks. uforarbejdede sojabønner kun har værdien 0.91, sorte bønner ligger på 0.75, andre bælgfrugter har 0.70, peanuts har 0.52, og hele hvedekerner opfylder kun proteinbehovet til en karakter på 0.42.. Der er dog tilsyneladende mindre forskelle i hvilke resultater de enkelte laboratorier opnår, selvom de tester det samme sojamateriale, og PDCAAS værdierne svinger mellem 0.92 og 1.00. Det amerikanske soja eksport råd lover da heller ikke mere end at PDCAAS værdien er over 0.9. Generelt må man forvente at isolerede soja proteiner leverer alle de aminosyrer man har behov for.

*Soy4you® og Soy4you øko® indeholder alle de nødvendige aminosyrer i tilstrækkelige mængder til at kroppen ikke behøver andre proteinkilder.*

## 5. Helbredseffekter af sojaindtag

### 5.1. Generelle kommentarer

*Et moderat og velafbalanceret indtag af sojaprodukter kan have positive effekter på helbredet, mens et overdrevet og ubalanceret indtag af soja kan have uønskede virkninger på mennesker med allerede udviklede sygdomme, genetiske prædispositioner og ubalancer i kroppen.*

Læser man om sojas helbredsvirkninger, støder man både på en række publikationer og hjemmesider, der indeholder nogle meget rosende omtaler af virkningerne, men man støder også nogle ret heftige modargumenter mod at spise soja. Grunden til heftigheden i argumenterne skal nok findes i, at specielt i det amerikanske samfund har soja været udråbt som en ”Mirakel fødevarer”, både af medierne og af sojaindustrien. Dette har medført, at en del mennesker i et misforstået ønske om at være ekstra sunde har valgt at basere en uforholdsmæssig stor del af deres diæt på sojaprodukter. Argumenternes heftighed bør derfor nok opfattes som en lettere overdramatiseret advarsel mod alt for ensidigt at bruge soja som sin daglige proteinkilde. Studerer man de videnskabelige undersøgelser på området, finder man primært indicier på at et overdrevet sojaindtag kan have uønskede effekter, mens et afbalanceret indtag primært har positive effekter og effekter på allerede udviklede sygdomme, genetiske prædispositioner og ubalancer i kroppen.

Debatten om hvorvidt visse sojaprodukters indhold af hormonlignede molekyler har en indflydelse på udviklingen af bl.a. brystkræft raser frem og tilbage i de videnskabelige kredse. Sojaindustrien har en klar interesse i at styre debatten, og en gruppe videnskabsfolk knyttet til kommercielle interesser argumenterer heftigt for de gavnlige effekter, mens andre mere moderate videnskabsfolk ser mere kritisk på den samlede viden fra humane forsøg. Et langt stykke hen ad vejen argumenterer begge ”leje” ud fra de samme videnskabelige undersøgelser, og kan med rette gøre det, da specielt humane forsøg ofte er meget komplekse og kan tolkes i flere retninger. Grunden til dette er, at humane forsøg er meget svære at udføre på en standardiseret måde, da man sjældent kan styre og verificere nøjagtigt hvad de deltagende mennesker faktisk indtager og gør, udover at indtage den foreskrevne mængde soja. I cellekulturer og dyreforsøg kan man derimod styre alle parametre helt nøjagtigt, og kan derfor f.eks. give meget ensidige diæter til rotter der er fremavlet til at være kraftigt disponerede for at udvikle kræft. Men disse resultater kan ikke nødvendigvis overføres til mennesker, der lever i en hverdag, hvor de udsættes for forurening, pesticidrester og alle mulige andre potentielle sygdomsfremkaldende stoffer. Så for at få en indsigt i hvad den almindelige forbruger kan forvente af effekt af at indtage sojaprodukter, vil vi her fokusere på humane forsøg.

*En stor del af de indholdsstoffer der kan være årsag til både de helbredsmæssigt gavnlige og uønskede effekter er fjernet i Soy4you®, mens en større del er bevaret i Soy4you øko®.*

## 5.2. Hormonregulerende effekter af isoflavoner

*Isoflavoner, som findes i mange sojaprodukter, har i menneskekroppen en beviselig påvirkning på mange østrogenstyrrede processer.*

Isoflavoner tilhører stofgruppen phytoøstrogener, som forekommer naturligt i soja og i en lang række andre plantebaserede fødevarer, såsom nødder, korn, ris, æbler og mange andre. Phytoøstrogeners primære effekt i menneskekroppen ligger i, at de har affiniteter til nogle af de samme bindingssteder som østrogen. Derfor vil phytoøstrogener optaget i kroppen ”konkurrere” med østrogen om mulige bindingssteder, og i tilfælde af lave østrogenmængder vil phytoøstrogenerne nogle steder kunne få kroppen til at opfatte en højere mængde østrogen, end der faktisk er i kroppen. Forskning har dog vist, at selvom der er fællestræk mellem den virkning som henholdsvis isoflavoner og østrogen har i kroppen, så er der distinkte forskelle på bl.a. hvilke gener de påvirker i organismen, og man kan derfor ikke sætte direkte lighedstegn mellem de to stofgrupper.

Hormonniveauer og -balancer har stor betydning for mange af kroppens processer, både på et dagligt plan og på længere sigt. En del sygdomme og andre kropslige uensigtsmæssigheder kan udløses eller forværres af ubalance i kroppens hormonbalance. Soja bønners indhold af bl.a. det hormonlignende molekyle Genistein, gør, at de potentielt kan have både positive og negative virkninger på hormonbalancen i den menneskelige organisme.

De mest omdiskuterede effekter ved indtagelse af isoflavoner centrerer sig omkring muligheden for påvirkning af kolesterolsammensætningen, kvinders brystkræftsrisiko, mænds prostatakræft, ubehag under kvinder overgangsalder, knogleskørhed, forplantningsevnen og børns udvikling.

*En stor del af isoflavonerne er fjernet i Soy4you®, mens en større del er bevaret i Soy4you øko®.*

## 5.3 Soja og brystkræft

*Undersøgelser har vist at der ikke er statistisk belæg for at sige at isoflavoner beskytter mod brystkræft, men at de sandsynligvis hæmmer videreudviklingen af brystkræft.*

I et stort studie blev ca. 200.000 mennesker af mange forskellige etniske afstamminger fulgt gennem en længere årrække, og deres diæter og sygdomshistorier blev nøje registreret og analyseret for en mængde sammenhænge(11). Af disse blev 3842 udvalgt og analyseret, fordi de var over 50 år, og blev diagnosticeret med brystkræft undervejs i forsøgsperioden. Konklusionen var at mængden af soja i kosten hverken havde en statistisk signifikant betydning for den brystkræftrelaterede dødsfrekvens eller for længden af sygdomsforløbene. Dog sås der indenfor enkelte etnicitetsgrupper en tendens til livsforlængende effekter. Dette ligger på linje med en stribe mindre studier på amerikanske og kinesiske befolkningsgrupper (7,8, 22,25, 39). Statistisk set kan man hermed ikke sige om soja har en direkte indflydelse på diagnosticeringen af brystkræft, men at sojaindtag sandsynligvis har en positiv indflydelse på forløbet af sygdommen.

*En stor del af isoflavonerne er fjernet i Soy4you®, mens en større del er bevaret i Soy4you øko®.*



## 5.4. Soja og prostatakraft

*Undersøgelser har primært vist marginalt positive effekter af soja mod prostatakraft*

Isoflavoner fra soja akkumuleres i prostata kirtlen og det er påvist at isoflavoner kan påvirke en række af de hormoner der er relevante for udviklingen af prostatakraft (23). Det er desuden påvist at isoflavoner har en indvirkning på udtrykket af visse gener og på andre mekanismer, der indvirker på kræftens udvikling (26, 27). Dog viser en samlet vurdering af en række menneskelige befolkningsstudier at deciderede signifikant påviste virkninger af soja på udviklingen og fremskridningen af prostatakraft er forholdsvis sjældne, og at de fleste studier kun viser marginale positive effekter (1, 36).

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## 5.5. Soja og overgangsalder

*Effekten på overgangsalder symptomer er blandt sojasprodukters bedst videnskabeligt dokumenterede helbredseffekter*

I forbindelse med overgangsalderen (klimakterium) holder æggestokkene op med at producere østrogen, og det har flere indvirkninger på kroppens væv og funktioner. Bl.a. oplever mange kvinder hedeture, hjertebanken, tørre slimhinder i skeden og hyppigere knoglebrud. Isoflavoner fra sojabønner og andre østrogenlignende phytoøstrogener fra f.eks. rødkløver har gennem mange generationer været brugt af kvinder mod ubehag under og efter overgangsalderen, og moderne videnskabelige undersøgelser har vist at effekten er reel.

Knogler er ikke blot døde kalkstænger, der holder struktur på kroppen, men indeholder levende celler der hele tiden opbygger og nedbryder knoglevæv. Det er det, der bl.a. gør at knoglebrud kan hele. Balancen mellem de knogle-nedbrydende og opbyggende cellers aktivitet er styret af mange forskellige faktorer, bl.a. mængden af østrogen. Derfor kan balancen påvirkes ved at indtage østrogenlignende phytoøstrogener fra soja, som primært hæmmer aktiviteten af de knoglenedbrydende celler (32).

Et større antal videnskabelige undersøgelser, både på større og mindre befolkningsgrupper, viser resultater der svinger lige fra ingen til betydelige effekter af indtagelse af isoflavoner på knogletilstanden og tilhørende biologiske markører i kvinder i og efter overgangsalderen (19). Resultaterne viser en forholdsvis stor spredning i effekterne, og for en stor del af studierne vedkommende kan det formodentlig tilskrives, at mange andre faktorer end sojaindtaget, såsom rygning og motion, spiller ind på knoglernes tilstand. Flere forskere, påviser en dosis-respons afhængig effekt, og viser at isoflavoner kun har effekt på knoglenedbrydningen, hvis personerne samtidig indtager tilstrækkeligt med kalk i diæten (32). Da visse sojaprodukter har en tendens til at kortvarigt nedsætte kalkoptagelsen i kroppen (se afsnit om mineraloptagelse), understreger det vigtigheden af at indtage soja som en del af en afvekslende kost.



Effekten af isoflavover på andre overgangsalderrelaterede symptomer, såsom hedeture, hjertebanken, tørre slimhinder i skeden, er ligeledes blevet undersøgt i et stort antal videnskabelige undersøgelser (19). Der hersker ikke en generel videnskabelig enighed om, hvordan isoflavonerne påvirker symptomerne, og resultaterne veksler mellem ingen og mærkbare effekter. F.eks. viser en stribe forsøg, at i sammenligninger mellem medicinske hormonbehandlinger og behandlinger med isoflavoner, at begge grupper havde positive effekter i livskvaliteten, sammenlignet med kvinder der ikke modtog behandling (6, 44). Dog er der ikke belæg for at konkludere, at der sås en ekstra øget effekt ved kvinder der indtog både medicinske hormonbehandlinger og behandlinger med isoflavoner. Derimod hævder andre at eventuelle virkninger af isoflavover på livskvaliteten hos kvinder i overgangsalderen primært kan tilskrives forskelle i etnisk afstamning, og de deraf følgende forskelle i diæt i løbet af livet.

*En stor del af isoflavonerne er fjernet i Soy4you®, mens en større del er bevaret i Soy4you øko®.*

## 5.6. Soja og forplantningsevne

*Ingen videnskabelige undersøgelser har påvist skadelige effekter af et moderat sojaindtag på hverken kvinder eller mænds fertilitet. Et moderat indtag af soja har ikke kunne påvises at påvirke hverken fostre eller spædbørn, dog bør gravide kvinder sandsynligvis være varsomme med overdreven indtagelse af isoflavoner.*

Selvom isoflavoner og andre phytoøstrogenener på mange måde minder molekylært om østrogen, virker de på lidt forskellige måder i den menneskelige organisme. F.eks. binder genestein sig ca. 30 gange dårligere til det ene af østrogens bindingssteder, ER $\beta$ , end til det andet, ER $\alpha$ . Da ER $\beta$  er det primære østrogenbindingssted i den mandlige prostatakirtel, som producerer størsteparten af sædvæsken, og styrer en stor del af den mandlige forplantningsevne, er det forventeligt at isoflavoner har en relativt mindre indflydelse på mænds end kvinders forplantningsevne. Antallet af studier af phytoøstrogeners effekt på mænds fertilitet er begrænset, og der er ingen samstemmende resultater, der peger i retning af hverken en hæmmende eller en fremmende effekt (9). En del studier på mus og rotter tyder dog på, at en livslang indtagelse af store mængder phytoøstrogenener kan have en negativ effekt på hanners kønsudvikling og fertilitet.

Hos kvinder er virkningen af indtagelse af isoflavoner på reproduktionsevnen noget mere velundersøgt end hos mænd, og i en sammenkædning af alle de kendte undersøgelser undersøgte sammenhængen mellem sojaindtag og forskellige kønsrelaterede hormoner og faktorer hos kvinder i den fødedygtige alder. Resultaterne viste at sojaindtag sandsynligvis ikke direkte påvirker kroppens egne østrogenniveauer, men kan have svage effekter på flere af de hormoner og faktorer, der er associeret med menstruationscyklussen, og at sojaindtag kan være koblet til en svag forlængelse af menstruationsperioden (9). Resultaterne viste ingen gennemgående sammenhæng til hverken øget eller sænket evne til at blive gravid eller frekvensen af misdannelser eller spontane aborter. Toksikologiske dyreforsøg med mus og rotter har vist at udsættelse for større mængder af phytoøstrogenener kan fremprovokere forskellige fysiologiske ændringer i reproduktionsorganerne. Blandt landmænd kendes begrebet ”kløversyge”, hvor drægtige dyr, der næsten udelukkende lever

af kløver, og derved udsættes for ekstreme mængder af phytoøstrogener, har en øget frekvens af drægtighedsproblemer, og at vædderlammene sidenhen har en ringere evne til at bedække. Så fødedygtige kvinder bør sandsynligvis ikke basere hele deres diæt på isoflavon-rige sojaprodukter, men nøjes med at lade sojaprodukter være en del af en varieret diæt (9).

*En stor del af isoflavonerne er fjernet i Soy4you®, mens en større del er bevaret i Soy4you øko®.*

### **5.7. Effekt af soja på graviditet og børns udvikling**

*Et moderat indtag af soja har ikke kunne påvises at påvirke hverken fostre eller spædbørn*

Foster- og spædbørnstiden er kritisk for udviklingen af en mængde forskellige fysiske træk ved det voksne menneske. Specielt kønsudviklingen er ømfindelig, og der har været rejst en del bekymring over eventuelle effekter af fytohormoner i både den gravide moders og spædbørnens diæt. En gennemgang af den eksisterende videnskabelige viden på området viser dog at der ikke er grund til bekymring, da resultaterne forholdsvis samstemmende ikke viser en øget frekvens af anormaliteter ved et moderat indtag af soja. Dog viste en undersøgelse af en gruppe vegetarers forholdsvis høje indtag af soja under graviditet en svagt øget frekvens af drenges deformiteter i kønsorganer. Tilfældene var dog også knyttet til både tilfælde af influenza tidligt i graviditeten og til manglende jerntilskud (35). Isoflavoner overføres kun i meget ringe mængde til modermælken, så ammende kvinder bør ikke afholde sig fra at inkludere soja i en varieret diæt (5).

Sojabønnen har en del ernæringsmæssige kvaliteter, der gør den velegnet som ingrediens i bl.a. modermælkserstatning, og soja har i over 40 år rutinemæssigt været brugt til spædbørn i store dele af den vestlige verden. Et større antal studier af effekten af soja i modermælkserstatninger hos piger viser samlet set meget få eller ingen bivirkninger eller ændringer i f.eks. tidspunktet for starten på pubertet og reproduktive egenskaber, selvom et par studier f.eks. fandt en svagt øget risiko af have længere menstruations-perioder og -smerter og for livmoderfibromer hos voksne kvinder der indtog soja som spæde (12, 41).

Hos drenge viser forskningen samlet set også meget få eller ingen bivirkninger eller ændringer i f.eks. tidspunktet for starten på pubertet og reproduktive egenskaber. En lang række dyreforsøg viser samlet set også meget få tendenser til ændrede udviklings- og livsforløb ved indtagelse af soja i den spæde alder.

*En stor del af isoflavonerne er fjernet i Soy4you®, mens en større del er bevaret i Soy4you øko®.*

### **5.8 Effekten af soja på sammensætningen af kolesterol i kroppen**

*Indtagelse af soja har en veldokumenteret positiv effekt på sammensætningen af kolesterol i kroppen*

Det er nu klart at f.eks. risikoen for hjerte-karsygdomme er nøje knyttet til sammensætningen af kolesterol i kroppen og i føden (18). Kolesterol er lipider som i sig selv er uopløselige i blod, men som kan transporteres rundt i kroppen, hvis de bindes til forskellige lipoproteiner. I relation til

sundhed, deler man ofte kolesterol op i ”gode” kolesteroler, HDL (Høj Densitets Kolesterol) og ”dårlige” kolesteroler, LDL (Lav Densitets Kolesterol). Høje niveauer af LDL er knyttet til øget risiko for hjerte-karsygdomme. Kolesterol dannes både i kroppen selv, og tilføres med den indtagne mad.

En lang række undersøgelser har vist at indtagelse af soja kan bevirke at mængden af det dårlige LDL kolesterol sænkes i blodbanen, mens mængden af det gode HDL kolesterol forbliver uændret (21, 28, 29). Mekanismerne der styrer denne effekt er endnu ikke forstået til fulde, og er sandsynligvis koblet til flere elementer i soja. Det ligger dog klart at visse sojaproteiners evne til at binde sig til kolesterol og indholdet af fibre og isoflavoner spiller vigtige roller.

De amerikanske sundhedsmyndigheder har anerkendt soja som en kur mod forhøjede værdier af kolesterol, mens de europæiske myndigheder endnu ikke mener at der er entydige beviser nok (18, 21). Og ikke mindst har det en betydning, at mange animalske proteiner har en decideret kolesterolhævede effekt på kroppen, så hvis man helt eller delvist erstatter sit indtag af animalske proteiner med sojaproteiner, får man en samlet sænkning af de dårlige kolesteroler i kroppen.

*Specielt fedtreducerede soja produkter, såsom Soy4you® og Soy4you øko® har en positiv effekt på sammensætningen af kolesterol i kroppen*

### **5.9. Soja og mineraloptagelse**

*Videnskabelige undersøgelser viser, at balancerer man sit indtag af sojaprodukter med andre fødekilder udlignes risikoen for mineralmangel*

Soja og en lang række andre plantebaserede fødevarer indeholder phytater og oxylater, der er ufordøjelige i den menneskelige organisme, og som reducerer kroppens mulighed for at optage vigtige mineraler, såsom kalk, jern, magnesium og zink. Varmebehandlingen af Soy4you’s produkter reducerer mængden af phytater og oxylater, og videre varmemeforarbejdning under tilberedning vil yderligere mindske påvirkningen af mineraloptaget. Undersøgelser har vist at eventuelle midlertidige nedsættelser i mineraloptaget i forbindelse med sojaindtag hurtigt udlignes ved indtagelse af andre fødevarer og mineraltilskud (30). Det er derfor vigtigt at give kroppen hyppige pauser i sojaindtagelsen, således at mineralbalancen kan opretholdes.

*Varmebehandlingen af Soy4you’s produkter reducerer mængden af phytater og oxylater, der forstyrrer mineraloptagelsen*

## 5.10. Soja og allergi

*Soy4you's produkter gennemgår en varmebehandling ved relativt høje temperaturer, hvorved en del af de allergifremkaldende proteiner slås i stykker.*

I Danmark er sojaallergi ikke særlig udbredt (mindre end 0,7% hos voksne og 1,4% små børn) (40). Hos børn er der god udsigt til at vokse fra sojaallergi. Men allergi overfor fødevarer er et reelt problem, og man bør altid være opmærksom på kroppens respons på de fødevarer man indtager.

Rå soja indeholder omkring 33 proteinvarianter, der potentielt kan give allergiske reaktioner (4). Varme- og trykbehandling ødelægger dog helt eller delvist de dele af proteinerne, der minder om kroppens egne immunoglobulin E antistoffer, som kan bindes til receptorer på mastceller og udløse allergi. Varmebehandlede sojaprodukter, såsom Soy4yoy's, giver derfor en lavere risiko for at udvikle allergi imod soja.

Sojabønner er en bælgfrugt. Ved allergi over for soja får nogle derfor også allergiske symptomer, når de spiser andre bælgfrugter, fx grønne ærter, bønner, linser eller jordnødder. Årsagen er, at proteinerne i fødevarerne ligner hinanden, og at kroppen reagerer, fordi den ikke kan skelne mellem de allergifremkaldende stoffer. Det kaldes en krydsreaktion, som giver de samme symptomer, som når man spiser soja, men ikke alle med allergi over for soja oplever krydsreaktioner. Den eneste sikre måde at undersøge, om du reagerer på soja, er at få foretaget en provokation hos lægen.

*Varmebehandlede sojaprodukter, såsom Soy4yoy's, giver derfor en lavere risiko for at udvikle allergi imod soja.*

## 5.11. Metabolisme relaterede effekter af soja indtagelse

*Trypsin hæmmerne ødelægges ved varmebehandlingen og findes derfor ikke i Soy4you® og Soy4you øko®. Isoflavoner og purin kan have negative effekter på mennesker med gigt og skjoldbruskkirtel problemer*

Fra naturens hånd er sojabønningen et levende frø, der har til formål at kunne spire og danne en ny sojabønneplante. Til det formål har bønningen oplagret en del energi i form af proteiner, fedt og sukkerstoffer. Men bønningen er ikke interesseret i at energien udløses før den er klar til at spire. Derfor findes der i frøet en stribe forskellige molekyler der bl.a. hæmmer de enzymer der nedbryder proteiner (trypsin inhibitorer). Trypsin er kroppens vigtigste enzym til nedbrydning af proteiner i tarmen, og det er derfor uheldigt, hvis bønnens naturlige fordøjelseshæmmere forhindrer virkningen af enzymet. Soy4You's produkter (både Soy4you® og Soy4you øko®) har dog gennemgået en varmebehandling, der effektivt har inaktiveret trypsin inhibitorerne, således at tarmens enzymer kan fungere fuldt ud normalt.

Sojabønner indeholder moderate til større mængder af purin, som også findes i næsten alle andre fødeemner. Hvis man indtager store mængder af purin i kosten, kan man forværre gigtsymptomer. Isoflavoner har vist sig at kunne hæmme skjoldbruskkirtlens funktion ved at påvirke iod-optagelsen. Dette kan forårsage en forøgelse af skjoldbruskkirtlen, som igen kan medføre lidelsen struma.

Endvidere er det vist at isoflavoner kan hæmme optagelsen af kunstige hormoner, men dette er dog vist for mange andre fødevarer, og hvis man indtager hormonerne efter forskrifterne og derudover sørger for at opretholde en fornuftig iod-balance, kan man fint indtage soja som en del af en balanceret kost (34).

De store mængder af uopløselige fibre i sojabønner virker rigtig godt på fordøjelsen og reducerer kolesterol i blodet og hæver tolerancen overfor sukker og gør cellerne mere reaktive på insulin. Det betyder at sojabønner også er godt i tilfælde af forstoppelse, diarré, for højt kolesterol og diabetes.

*En stor del af isoflavonerne er fjernet i Soy4you®, mens en større del er bevaret i Soy4you øko®.*

## **6. Sojas egenskaber i relation til forskellige befolkningssegmenter**

*Isolerede soja proteiner er ”halvhurtige” proteiner, som både favoriserer opbygning af muskelmasse og vedligeholdelsen af andre kropsfunktioner*

Motivationen for at indtage sojaproteiner afhænger kraftigt af den enkeltes behov og ønsker. Nogle spiser soja for at drage nytte af nogle af de mange sundhedsfremmende og sygdomshæmmende egenskaber ved soja. Andre spiser soja proteiner for at bygge eller restituere deres muskler efter hård træning. Nogle spiser soja for at tabe sig eller tage på efter sygdom, underernæring eller appetitløshed. Andre igen spiser soja af religiøse eller etiske grunde. Og endelig er der en stor befolkningsgruppe der simpelthen spiser sojaprotein fordi de kan lide smagen og har et ønske om at erstatte andre protein kilder med sojaprotein af og til.

*Bodybuildere og sportsfolk* For at levere toppræstationer eller for at reducere fedtprocenten i kroppen, lever mange sportsfolk og bodybuildere efter strengt kontrollerede diæter, og mange benytter sig af protein pulvere som deres hovedkilde til protein. Hovedkilderne til disse proteiner er mælke-valle, mælke-kasein, æg, kød og soja. En del undersøgelser har vurderet forskellene mellem de forskellige kilder, og hovedkonklusionen er at hastighed hvormed proteinerne fordøjes og optaget har en afgørende betydning for den resulterende muskelopbygning (15, 38, 42). ”Hurtige” proteiner, såsom mælke-valle proteiner er svagt overlegne til at stimulere muskelopbygning, men underlegne til at levere aminosyrer til resten af kroppens behov, dvs. opbygning og vedligeholdelse af vigtige organer såsom tarmvæv, hud, lever, etc. ”Langsomme” proteiner, såsom kød- og æggeproteiner er derimod ringere til at stimulere muskelopbygning, men bedre til at forsyne den øvrige krop med aminosyrer. ”Halvhurtige” proteiner”, såsom mælke-kasein og soja proteiner favoriserer både opbygningen af muskelvæv og forsyner resten af kroppen med aminosyrer på en balanceret måde (15, 38, 45)).

*Vægt-øgere* Nogle mennesker har et akut behov for at øge deres vægt eller for at opretholde et tilstrækkeligt højt niveau af aminosyrer i deres blod, men mangler evt. appetitten eller motivationen til at spise. Dette gælder anorektikere, svage ældre, hospitalsindlagte mennesker, kemopatienter, fejlnærede børn, mennesker med dysfunktionel metabolisme eller fordøjelse, etc. For mange af disse gælder det at manglede appetit eller aminosyre-optag i kroppen gør at den indtagne føde ikke dækker kroppens behov, og det er derfor vigtigt at få ”noget for pengene” med den føde det faktisk

lykkes at spise. Sammenlignet med fedt og kulhydrater, har proteiner en tendens til at skabe mæthedsfølelse hurtigere, og dermed manglende lyst til at spise mere (3, 31, 33, 43). Derfor kan isolerede ”halvhurtige” proteiner levere en koncentreret kilde til komplette proteiner til småt-spisende. Ved hospitalsindlagte ældre er der en høj risiko for forskellige følgelidelser, og i et studie hvor mælke-kasein og soja blev sammenlignet, sås det at sojaspisende havde en signifikant mindre risiko for at udvikle liggesår, tarmproblemer, og gå bort end ved kaseinindtagelse (20). Soja protein har et højt indhold af leucin, som har vist sig at være en afgørende faktor ved muskelopbygning og vægtforøgelse hos cancerpatienter i bedring (16).

*Vægt tabere* Overvægt er et problem for et stigende antal mennesker. At spise fedtreducerede produkter, såsom isolerede soja proteiner har den åbenlyse fordel at man får dækket sit aminosyrebehov uden at indtage så meget fedt som hvis man f.eks. indtager dem i form af kød. Derudover har soja proteiner vist sig at skabe mæthedsfølelse hurtigere end andre proteinkilder, såsom valle- og kasein-proteiner fra mælk, og derved potentielt reducere de samlede fødeindtag (3). Stigningen i det glykemiske og insulinemiske index i blodbanen giver en indikation af hastigheden hvormed blodsukkeret stiger efter indtagelsen af en fødekilde. En for hurtig stigning forøger risikoen for at overskudsenergi deponeres som lagerenergi (f.eks. i fedtceller) i stedet for at blive brugt til metabolistiske formål, og dermed forøger risikoen for en vægtforøgelse. Morgenmad indeholdende soja protein sammenlignet med en standard proteinrig morgen mad resulterede i signifikant langsommere stigning i det glykemiske index (31).

*Vegetarer* Vegetarer, veganere og andre har valgt primært at basere deres protein indtag på plantebaserede fødekilder. Dette giver dem en vis udfordring i at optage alle de nødvendige aminosyer i tilstrækkelige mængder, idet visse aminosyrer er relativt sjældne i planter. Isolerede soja proteiner er et ”komplet protein”, og leverer hermed alle de nødvendige aminosyrer. Men da visse sojaprodukter tillige indeholder bl.a. fytansyrer, som kan nedsætte optagelsen af visse mineraler, har vegetarer en ekstra udfordring med at opretholde en sund mineralbalance. Isolerede soja proteiner indeholder dog kun ganske små mængder fytansyre, og et normalt mineraloptag kan nemt opretholdes ved en varieret kost indeholdende soja protein. (34).

*Mennesker med sygdomme og lidelser* Selvom den etablerede medicinalverden er tilbageholdende med at anerkende soja som en potentiel kilde til helbredelse og forebyggelse af en lang række sygdomme og lidelser, indtager et stadig voksende antal mennesker forskellige soja produkter af medicinske eller forebyggende årsager. Visse lidelser, såsom forhøjet kolesteroltal, knogleskørhed, ubehag ved overgangsalderen og hjertekarsygdomme er, af specielt de amerikanske sundhedsmyndigheder vurderet til at kunne afhjælpes ved et dagligt indtag af visse sojaprodukter

*”Normale” mennesker* Folk fra Østasien har indtaget sojaprodukter som en del af deres basale føde gennem årtusinder, og i løbet af de sidste årtier har resten af verdens mennesker gradvist øget deres soja indtag. En stor del af sojaen er ”skjult” som ingredienser i industrielt fremstillede fødevarer, børnemad, etc., men en voksende andel spises fordi forbrugere bevidst vælger soja i stedet for andre proteinkilder. Det kan godt være at soja ikke er den ”mirakelfødevarer” som nogle amerikanske



fortalere gerne vil have os til at tro, men det er unægtelig at soja protein er en sund, fedtfri kilde til et komplet protein, som i mange retter fint kan erstatte kød.

*Soy4you® og Soy4you øko® er fedtreducerede isolerede proteiner, der leverer en balanceret kilde til sunde proteiner*

## **7. Miljømæssigt bæredygtige proteiner fra soja**

*Produktionen af soja protein har en langt mindre miljømæssig påvirkning end produktionen af animalske proteiner*

Det vil i fremtiden være nødvendigt at erstatte animalske proteiner og øge udnyttelsen af planteproteiner i en verden hvor protein behovet er stadig stigende. Selvom planteproteiner er relativt billige og kan produceres i store mængder uden at belaste miljøet så meget, er brugen af disse til direkte menneskeføde endnu begrænset. Størstedelen af den producerede mængde planteproteiner bruges nu til at fremavle mælk, æg og kød. (13). Men konverteringen af planteproteiner til animalske proteiner er ret ineffektiv, idet kun 10-15 % af de forbrugte planteproteiner kan ”høstes” igen fra dyrene, og dermed ”spildes” de resterende 85-90% af planteproteinerne (2, 37). Derfor står produktionen af dyreprotein for en uforholdsmæssig stor del af den miljømæssige belastning ved fødevarerproduktionen i verden (14, 24). Arealmæssigt kan det samme areal brødføde 10 gange så mange mennesker der lever af planteproteiner, som mennesker der lever af dyreproteiner, og dertil kommer, at i forhold til en mængde planteprotein, koster det ca. 100 gange så meget vand at producere den samme mængde kød (14). Endvidere står verdens kvægbestande for en betragtelig del af den globale udledning af drivhusgasser, primært i form af metan, så der er mange gevinster at høste ved at overgå til at spise plante proteiner (15). Soja proteiner leverer alle de nødvendige aminosyrer til den menneskelige organisme, og tilbyder derfor et sundhedsmæssigt og bæredygtigt alternativ til animalsk baserede proteinkilder (13).

*Soy4you® og Soy4you øko® er produceret så det umiddelbart kan erstatte animalske proteiner i mange dagligdags retter*



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# Literature review on aspects of human consumption of soy

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## Preface

The aim of the present paper is to provide a critical review of the existing knowledge and literature on the characteristics, potential beneficial and detrimental effects, and general knowledge of human consumption of soy products. Many aspects of the review will focus on human soy consumption in general; however special emphasis will be put on isolated soy proteins (ISP), and the textured ISP products of *Soy4 you* in particular.

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2. Content of soy
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## 1. Introduction to soy and human consumption of soy

*Soy products are gradually gaining ground on the dinner tables, and can in the long run become healthy environmentally sustainable replacements for many meat products*

The soybean (*Glycine max*) is a legume species native to East Asia, widely grown for its edible bean which has numerous uses. It is now grown commercially in many parts of the world, and soybeans are a globally important crop, providing oil and protein. Soybean is now the world's fourth most important crop, only surpassed by wheat, maize and rice. The bulk of the harvest is solvent-extracted, and the defatted soymeal (50% protein) makes the raising of farm animals possible on an industrial scale never before seen in human history. A relatively small proportion of the crop is consumed directly by humans.

In East Asia Soy has been consumed for centuries in many forms. In China, Japan, and Korea, soy products made are popular parts of the diet. The Chinese invented tofu and also made use of several varieties of soybean paste as seasonings. Japanese foods made from soya include miso, natto, kinako and edamame. Also many kinds of food are produced using tofu such as atsuage, aburaage, and so on. In Korean cuisine, soybean sprouts, called kongnamul, are also used in a variety of dishes, and are also the base ingredient in doenjang, cheonggukjang and ganjang. In Vietnam, soybeans are used to make soybean paste, tofu, soya sauce, soya milk.

The beans can be processed in a variety of ways. Common forms of soy include soy meal, soy flour, soy milk, tofu, textured soy protein (TSP), which is made into a wide variety of vegetarian foods, (some of them intended to imitate meat), tempeh, soy lecithin and soybean oil. Soybeans are also the primary ingredient involved in the production of soy sauce.

## 2. Content of soy

*Soy beans have a relatively low content of fat and carbohydrates and a relatively high content of proteins, and furthermore contain a number of health promoting compounds*

Together, soybean oil and protein content account for about 60% of dry soybeans by weight (protein at 40% and oil at 20%). The remainder consists of 35% carbohydrate and about 5% ash. Soybean consists of approximately 8% seed coat or hull, 90% cotyledons and 2% hypocotyl axis or germ.

*Proteins* Raw soybeans primarily contain legume proteins belonging to the globulin family of seed storage proteins called legumins and vicilins, or in the case of soybeans, glycinin and beta-conglycinin. Soy protein is generally regarded as stored protein held in discrete particles called "protein bodies" estimated to contain at least 60% to 70% of the total protein within the soybean. This protein is important to the growth of new soybean plants, and when the soybean germinates, the protein will be digested, and the released amino acids will be transported to locations of seedling growth. Legume proteins, such as soy, belong to the globulin family of seed storage proteins called legumin (11S globulin fraction) and vicilins (7S globulin), or in the case of

soybeans, glycinin and beta-conglycinin. Soybeans also contain biologically active or metabolic proteins, such as enzymes, trypsin inhibitors, hemagglutinins, and cysteine proteases. The soy cotyledon storage proteins, important for human nutrition, can be extracted most efficiently by water, water plus dilute alkali (pH 7–9), or aqueous solutions of sodium chloride (0.5–2 M).

*Carbohydrates* Soybeans are relatively low in carbohydrates (35%), and nearly all the carbohydrates in soy are fibres and oligosaccharides. The principal soluble carbohydrates of raw soybeans are the disaccharide sucrose, the trisaccharide raffinose, and the tetrasaccharide stachyose. The oligosaccharides raffinose and stachyose are not digestible sugars in humans, and contribute to flatulence and abdominal discomfort, as undigested oligosaccharides are broken down in the intestine by native microbes, producing gases such as carbon dioxide, hydrogen, and methane. The insoluble carbohydrates in soybeans consist of the complex polysaccharides cellulose, hemicellulose, and pectin. The majority of the insoluble soybean carbohydrates can be classed as belonging to dietary fibres (Choi and Rhee, 2006).

*Oils* Raw soybeans contain app. 20% fat, and are thus relatively high in fat content. The major unsaturated fatty acids in soybean oil are the poly-unsaturated  $\alpha$ -linolenic acid (Omega-3)(7-10%), and linoleic acid (Omega-6)(50-60%) and the mono-unsaturated oleic acid (20-25%). It also contains the saturated fatty acids, stearic acid (3-7%) and palmitic acid (5-10%) (Choi and Rhee, 2006).

*Phytoestrogens* Soybeans contain different isoflavones and coumestans, and further contain plant lignans, which are the principal precursor to mammalian lignans. However, the isoflavone content of soy is usually attracting the largest attention. Phytoestrogens are primarily interesting in relation to human intake because they have the ability to bind to human estrogen receptors, and thus influence bodily actions normally governed by natural estrogen levels. However, phytoestrogens have furthermore been reported to act as inhibitors of tyrosine kinases, influence signal transduction pathways, act against oxidation of DNA, and enhance the activity of anti-oxidant enzymes in various organs (Isanga and Zhang, 2008).

*Isoflavones* are a group of naturally occurring heterocyclic phenols, which are present in soy bean at levels of 0.1 to 5 mg/g (Isanga and Zhang, 2008). The three major groups of isoflavones found in soybeans are genistein, daidzein, and glycitein, and the genistein and daidzein forms constitute the absolutely largest proportion of isoflavones in soy. Isoflavones can generally exist in soybeans as aglycones (daidzein, genistein, and glycitein), glycosides (daidzin, genistin, and glycitin), acetylglycosides (acetyldaidzin, acetylgenistin, and -acetylglycitin), and malonylglycosides (malonyldaidzin, malonylgenistin, and malonylglycitin). Isoflavones in the acetylglycoside and malonylglycoside form are not bioavailable for the human body, whereas the glycoside forms can be deglycosinated into the aglycone forms, which are absorbable in the human intestine (Isanga and Zhang, 2008). The deglycosination of the glycoside forms into the aglycone forms was previously thought to be mediated by colon microflora, but experiments have shown that it is mediated by enzymes in the intestinal cells (Nielsen and Williamson, 2007). The enzymatic conversion of the glycoside form is very dependent on - the vitality of the intestine cells, - whether other food items

compete for the enzymatic activity, - blood circulatory parameters, - etc. Another transformation of daidzein into the isoflaonoid equol is mediated by a specific microflora, however only an approximated 40% of the human population has this specific microflora in the intestine. Interestingly, a larger proportion of people from East Asia have this microflora than people of Western origin. All in all, the bioavailability of ingested isoflavones is thus depending on: - the ingested soy product, - which food the soy has been ingested along with, - the intestinal microflora, - and several other factors. This makes it very difficult to predict and standardize the absorption rate of biologically active isoflavones in e.g. human experiments, and to issue standardized recommendations for intake of isoflavones.

*Minerals* The mineral content of soybeans, determined as ash, is about five percent. When soybeans are processed, most of the mineral constituents go with the meal and few with the oil. The major mineral constituents are potassium, calcium and magnesium. The minor constituents comprise trace elements of nutritional importance, such as iron, zinc, copper etc. The biological availability of minerals may be impaired somewhat as a result of the presence of phytates in soybeans and soybean products.

*Antinutritional elements* Soybeans contain a number of elements which have unwanted or detrimental effects in the human organism. - *Phytic acid* or the salt form *phytate* acts as an antioxidant, and furthermore has a strong binding affinity to important minerals, such as calcium, iron, and zinc, although the binding of calcium with phytic acid is pH-dependent and ascorbic acid (vitamin C) can reduce phytic acid's effect on iron. When iron and zinc bind to phytic acid they form insoluble precipitates and are far less absorbable in the intestines. This process can therefore contribute to iron and zinc deficiencies in people who rely their mineral intake on food containing high amounts of phytic acid for. Simple cooking will reduce the phytic acid to some degree. More effective methods are soaking in an acid medium, lactic acid fermentation, and sprouting (Isanga and Zhang, 2008). - *Trypsin inhibitors* are molecules, which bind to the enzyme trypsin, and thereby inhibit the degradation of certain lipid bonds among amino acids (lysine and arginine) of proteins in the intestine of humans and animals. This prevents the uptake of amino acids, and further detrimentally affects the enzyme balance and may cause hypertrophic pancreas responses. Soy beans contain at least two types of trypsin inhibitors, and the biological function of the inhibitors is thought to be, that animals will avoid eating the raw beans in the long run (Selgrade et al., 2009). Heating, fermentation and leaching eliminates the activity of the inhibitors (Isanga and Zhang, 2008). - *Lectins* are a natural part of many legumes, and are toxic to humans at higher levels. In mature raw soybeans the lectin levels are low, whereas in green immature beans the levels may be higher. Lectins bind to the gut wall and reduce epithelial cell vitality and functionality, and thus inhibit the absorption of vital nutritional elements into the body. Possible beneficial effects of lectins, e.g. their anti-cancer effects, have, however, been debated in science (Isanga and Zhang, 2008). Leaching, cooking and (moist) heat treatment deactivates the lectins (Isanga and Zhang, 2008). - *Soluble carbohydrates* are broken down during fermentation, soy concentrate, soy protein isolates, tofu, soy sauce, and sprouted soybeans are without flatus activity. On the other hand, there

may be some beneficial effects to ingesting oligosaccharides such as raffinose and stachyose, namely, encouraging indigenous bifidobacteria in the colon against putrefactive bacteria

### 3. Methods of assessment of the nutritional value of proteins

Proteins are nitrogen-containing substances that are built by amino acids. They serve as the major structural component of muscles and other tissues in the body. In addition, they are used to produce hormones, enzymes, haemoglobin, and several other vital components. Proteins can also be used as energy; however, they are not the primary choice as an energy source. For proteins to be used by the body they need to be metabolized into their simplest form, amino acids. Twenty amino acids have been identified as needed for human growth and metabolism. Twelve of these amino acids (eleven in children) are termed nonessential, meaning that they can be synthesized by our body and do not need to be consumed in the diet. The remaining amino acids cannot be synthesized in the body and are described as essential, meaning that they need to be consumed in our diets. The absence of any of these amino acids will compromise the ability of tissue to grow, be repaired or be maintained (Hoffman and Salvo, 2004).

It is important to understand that proteins are complex molecules, and that different proteins sources and different forms of the same protein can possess differences in: - which amino acid they contain, - their water solubility, - their stability in acidic and alkaline solutions, and - how easily they are degraded and absorbed in the human body. Proteins are found in many plant products, but not all plant proteins contain all the essential amino acids (or not in adequate amounts) for the human body to sustain a natural metabolism. A protein source is called a “Complete protein” if it delivers all the protein related components a human body needs.

To standardize the comparison of protein sources, numerous methods exist to determine protein quality, such as – “protein efficiency ratio”, “biological value”, “net protein utilization”, and “protein digestibility corrected amino acid score”. - The *protein efficiency ratio* (PER) determines the effectiveness of a protein through the measurement of animal growth. This technique requires feeding rats a test protein and then measuring the weight gain in grams per gram of protein consumed. The computed value is then compared to a standard value of 2.7, which is the standard value of casein protein. Any value that exceeds 2.7 is considered to be an excellent protein source. However, this calculation provides a measure of growth in rats and does not provide a strong correlation to the growth needs of humans. - *Biological value* (BV) measures protein quality by calculating the nitrogen used for tissue formation divided by the nitrogen absorbed from food. This product is multiplied by 100 and expressed as a percentage of nitrogen utilized. The BV provides a measurement of how efficient the body utilizes protein consumed in the diet. A food with a high value correlates to a high supply of the essential amino acids. Animal sources typically possess a higher biological value than vegetable sources due to the vegetable source’s lack of one or more of the essential amino acids. There are, however, some inherent problems with this rating system. The BV does not take into consideration several key factors that influence the digestion of protein and interaction with other foods before absorption. The BV also measures a protein’s maximal potential quality and not its estimate at requirement levels. - *Net Protein Utilization* (NPU) is similar to the

BV except that it involves a direct measure of retention of absorbed nitrogen. NPU and BV both measure the same parameter of nitrogen retention, however, the difference lies in that the BV is calculated from nitrogen absorbed whereas NPU is from nitrogen ingested (Hoffman and Falvo, 2004).

- *PDCAAS* The most widely accepted method is *Protein Digestibility Corrected Amino Acid Score* (PDCAAS). In the PDCAAS analyses the targeted protein source is analysed and compared to a reference protein source to assess whether the amino acid profile meets the demand of essential amino acids and nitrogen in a hypothetical 2-5 years old child, which is believed to be the age group where the demand for the “Complete protein” is largest. Hereafter a correction is made for the actual digestibility of the protein, by feeding the protein to rats and analysing how much of the protein is recovered in the faeces, and finally the result is truncated to 100%. The PDCAAS results in a score from 0 to 1.00, where 1.00 indicates that the protein provides the “Complete Protein”, whereas e.g. the score 0.70 indicates that the source does not live up to the criteria of providing the adequate amounts of the protein related elements which a human body needs.

The method is recognised by many to currently be the best method, however critics emphasises that the method has certain flaws and sources of error (Schaafsma, 2000). Primarily the method is criticized for uncertainties about the actual amino acid and nitrogen needs of a 2-5 year old child, and whether the needs of this age group is representative for all age groups and phenotypes of humans (Sarwar, 1997). Moreover it is criticized that the method does not encompass the fact that the micro flora of the last part of the intestine metabolises a part of the amino acids and proteins, and that it therefore probably would be more correct to measure the amounts of amino acids and proteins at the transition between the small intestine and the colon (Schaafsma, 2000). Furthermore the analyses of rat faeces is not necessarily representative for humans, as the intestinal micro flora and the metabolic needs of rats are different than human, and that rats for example have a higher need for sulphur rich amino acids to maintain their fur production than humans (Schaafsma, 2000). Supporters of the method, however, claims that the method gives sufficiently covering results to declare the nutritional and efficiency of use of protein sources within a feasible economic frame for the analyses (WHO). Minor differences are however found between the results of individual laboratories, even though the same soy material is tested (Hughes et al., 2011).

The American Food And Drug Administration (FDA) and UN’s food and health organizations (FAO/WHO) recognizes the PDCAAS method to be the best current method to assess to which degree a protein source delivers the “Complete protein” (Hughes et al., 2011). In the European Union, EFSA expresses reservations about the method (EFSA, 2013), but does however not offer any alternative methodologies.

*PDI* The Protein Dispersibility Index (PDI) is a method of comparing the solubility of a protein in water, and is widely used in the soybean product industry to evaluate the protein quality before and after a specific industrial process. A sample of a specific refined soy product is ground, mixed with a specific quantity of water, and blended together at a specific rpm for a specific time. The resulting mixture and original bean flour then have their protein content measured using a combustion test

(see below), and the PDI is calculated as the percentage of the protein in the mix divided by the percentage in the flour. A PDI of 100 therefore indicates total solubility (Batal et al., 2000). It has been shown that the PDI can be affected, not only by the type of soybean used, but also by manufacturing processes (Batal et al., 2000).

**The Combustion Method** The combustion method involves burning a sample in an oxygen-rich atmosphere at high temperatures and analysing the resulting gases. This process has three stages. **Combustion:** Once the sample is weighed and purged of any atmospheric gases, it is heated in a high-temperature furnace and rapidly combusted in the presence of pure oxygen at about 1000°C. **Reduction and adsorption:** The combustion products, mainly carbon dioxide, water, nitrogen dioxide, and nitrogen gas, are collected and allowed to equilibrate. An aliquot of the gas mixture is passed over hot copper to remove any oxygen and catalytically convert nitrogen dioxide to nitrogen. The sample is then passed through a trap that removes carbon dioxide and water. **Quantification:** The total nitrogen is measured by thermal conductivity (Marco et al., 2002).

#### 4. Nutritional values of soy proteins

*Soy protein isolate is a “Complete Protein”, and thus contains all the protein related components to sustain normal growth in a 2-5 year old child.*

Soy protein isolate is one of the few plant sources of protein, which is claimed to be a “Complete Protein” (PDCAAS = 1.00) (Hughes et al., 2011; Hoffman and Falvo, 2004), and is thereby in line with egg white, and the milk proteins whey and casein (all with PDCAAS = 1), whereas e.g. raw soy beans and beef only have the score 0.92, black beans score 0.75, other legumes score 0.70, peanuts score 0.52, and wheat proteins are as low as 0.25 (Hoffman and Falvo, 2004).

However, different cultivars of soy bean have different compositions of amino acids and proteins, and thus the resulting nutritional values vary accordingly, and scores between 0.92 and 1.00 have been published on isolated soy proteins. (Hughes et al., 2011). Particularly the amounts of the sulphur rich amino acids methionine and cysteine may be too low in some cultivars, and thus reduce the PDCAAS score. The processing of the soy protein isolate may also influence several factors related to the PDCAAS values. Primarily, the temperature- and pressure treatments during the processes are critical, as e.g. the amino acid lysine is sensitive to high temperatures, and may be lost, resulting in lower PDCAAS values (Batal et al., 2000).

To be on the safe side, the American Soy Export council does not promise a higher PDCAAS value than 0.90 in soy protein isolates, although the values are usually closer to, or equal to 1.00.

Generally soy protein isolate can be expected to deliver all the amino acids and nitrogen, which the body needs, however it is always recommended to let ISP be part of a varied protein intake from several sources. The PDCAAS value of *Soy4 you®* has been analysed to be 1.00.



## 5. Effects on anti-nutritional elements of the processing of soy beans

*Soy product contain quite different amounts of health promoting and detrimental elements depending on the pre-processing of the products*

Raw soy beans contain a number of elements, which are unwanted, either because they cause anti-nutritional digestion- and absorption-effects, or because they are irritating or poisonous to the body. The unwanted elements include: - *Lectins*, which react with the carbohydrate component of cell membranes, potentially causing cell-injuries and -deaths, and adversely affect the gastrointestinal, immune, and other systems of humans; *Protease inhibitors*, which interfere with the digestion of proteins in the intestine; - *Phytates*, which tie up minerals like calcium, zinc, and iron. Thus, all soy products used for human consumption have to go through some degree of processing before they become healthy to consume.

*Maceration and boiling* The simplest traditional form of processing the raw or dried beans is maceration and boiling. If the process is performed balanced and adequately, it reduces the toxicity of the lectins, breaks down the protease inhibitors, and partially reduces the activity of the phytates (Karkle and Beleia, 2010). Most of the oils, isoflavones, sugars and proteins are not reduced by maceration and cooking.

*Soy milk* It is produced by soaking dry soybeans and grinding them with water, pressing the fluid out, and subsequently boiling and sieving the “milk” out. Most antinutritional elements are unchanged, compared to raw soybeans.

*Fermentation* Another traditional way of processing the soy beans is fermentation. The fermentation can be performed by many different microorganisms, but the most used are *Saccharomyces*, *Aspergillus* and *Lactobacillus*, degrading sugars into alcohol and lactic acid, respectively. The processes have different effects on the composition, depending on the duration and other factors, but generally the end product contains low amounts of lectins, phytates, and protease inhibitors. Many of the isoflavones, sugars and proteins are reduced or changed by fermentation.

*Soy meal* Soy meal is the material remaining after solvent extraction of oil from soybean flakes, with 50% soy protein content. The meal is 'toasted' (heat treatment with moist steam) and ground in a hammer mill (Lin et al., 2000).

*Soy flour* Soy flour is made from soybeans ground finely enough to pass through a fine mesh where special care is taken during desolventizing to minimize denaturation of the protein to retain a high protein dispersibility index (PDI), for uses such as food extrusion of textured soy protein. It is the starting material for production of textured soy protein (TSP), soy proteins isolate (SPI), and soy proteins concentrate (SPC) (Lin et al., 2000).

*Isolated Soy Protein* Edible ISP is derived from defatted (alcohol extracted or cold pressed) soy flour with a high Protein Dispersibility Index (PDI). The aqueous extraction is carried out at a pH



below 9. The extract is clarified to remove the insoluble material and the "supernatant" is acidified to a pH range of 4-5. The precipitated protein-curd is collected and separated from the whey by centrifuge. The curd is usually neutralized with alkali to form the sodium proteinate salt before drying. The ISP can be further refined by extruding the product into Textured Soy Protein Isolate (TSP).

*Soy protein concentrate* SPC is produced by immobilizing the soy globulin proteins while allowing the soluble carbohydrates, soy whey proteins, and salts to be leached from the defatted flour. The protein is retained by one or more of several treatments: leaching with 20-80% aqueous alcohol/solvent, leaching with aqueous acids in the isoelectric zone of minimum protein solubility, pH 4-5; leaching with chilled water (which may involve calcium or magnesium cations), and leaching with hot water of heat-treated defatted soy meal/flour. The SPC can be further refined by extruding the product into Textured Soy Protein Isolate (TSP).

*Textured Soy Protein* TSP is extruded from defatted (alcohol extracted or cold pressed) soy flour, or the refined products ISP or SPC. The flour/proteins can be extruded into various sizes and shapes (chunks, flakes, nuggets, grains, and strips), exiting the nozzle while still hot and expanding as it does so. During the process, the defatted thermoplastic proteins are heated to 150-200°C, which denatures them into a fibrous, insoluble, porous network that can soak up as much as three times its weight in liquids (Hill et al., 2006). Extrusion temperatures are typically 120-140°C (Lin et al., 2000). The process may further involve the addition of colouring and flavours (Deliza et al., 2002). Several factors in the process, including cooking temperature, moisture, pressure, product temperature at extrusion, and colouring agents are critical for the hardness, gumminess and chewiness of the product (Lin et al., 2000). The 7S and 11S subunits of soy proteins are major components for the texturization, and both start to unfold when heated above 100 °C and become totally unfolded at 140 °C (Lin et al., 2000). Soybean meal must be heat-treated in order to reduce or eliminate anti-nutritional factors, such as trypsin inhibitors and phytates, and here the heating and extrusion processes are critical. Under-heating results in high levels of anti-nutritional factors, such as trypsin inhibitors remaining in the processed soybean meal (Thomas et al., 1997). Over-heating can result in a significant reduction in the digestible amino acid content of the soybean meal by Maillard reactions, in which reactive sugars are bound to amino acids, particularly lysine (Jeunink and Cheftel, 1979). The resulting PDCAAS values are thus easily affected by any improper moisture, pressure, temperature and mechanical shear in the process (Singh et al., 2007), and it is very important to identify and aim at soybean meal that has been processed just right (the "Goldilocks" value). The extrusion process has a tendency to increase the amount of soluble fibres and to decrease the insoluble fibre content (Singh et al., 2007). Minerals are not directly affected by the processes; however changes in fibre composition, and decreasing effects on mineral binding components, such as pythates and tannins, have positive effect on the resulting human absorption of minerals (Singh et al., 2007). Phenolic compounds, such as the isoflavonic health related bioactive aglycone compounds genestein and daidzin are prone to decrease under too high temperatures, however the majority are transformed to the glycoside analogues, which are readily reversed to the

aglycone form by the micro flora in the human intestine, whereas a proportion may be transformed into the non-bioactive acetyl- and malonyl- forms. (Singh et al., 2007).

*Properly manufactured Textured Soy Protein, such as Soy4you® and Soy4you øko® contains no trypsin inhibitors, contains drastically lowered pythates, tannins, and lectins, and contains proteins which are easier to digest for the human organism.*

## **6. Health aspects of soy and ISP consumption**

*A moderate and balanced intake of soy products can affect the health in a positive way, whereas an excessive and unbalanced intake can have unwanted effects in humans with already developed diseases, genetic predispositions and unbalances in the body.*

### **6.1. General comments**

Reading popular information about the health aspects of soy, the impression is rather ambiguous, as some popular publications and homepages highly praise the health aspects soy, whereas others, in strong terms, warn against the intake of soy. The reason for the vehemence in the arguments probably has to be found in the fact that, particularly in the USA, soy has been shouted out as a “Miracle food”. In a misunderstood desire to be extra healthy, this has, in an unbalanced manner, led some people to base a very large part of their diet on soy based foods, or in other ways to exaggerate the intake of soy derived components, e.g. isoflavones. As the “American style” of argumentation is often rather overdramatized, the vehemence in the arguments should probably mainly be perceived as well meant warnings against an exaggerated intake of soy, whereas many of the exaggerated praising popular references should be taken as arguments for improved sale, and similarly taken with a grain of salt.

Reviewing the scientific literature, the picture is less dramatically ambiguous; however it is clear that when setting up experiments and hypotheses, some science groups have clearly had the goal to prove health benefits, whereas other have clearly had the goal to prove detrimental effects of soy. However the scientific integrity is intact in the majority of the present soy related science, and particularly some of the meta-analyses and collective reviews of many individual experiments provide reliable information on the health aspects of soy intake.

Scientific investigations of the health aspects of soy intake can roughly be divided in three sections: - *Human cohort studies*, where large groups of persons are followed for a time period, and are asked to report e.g. their specific food intake, income and social status, exercise level, and health history, - *Human intervention experiments*, where groups of specifically selected persons are asked to perform (eat/exercise/etc.) in a specific manner for a specific time period, - *Laboratory animal experiments*, where uniform groups of laboratory animals (often rats or mice) are used as human model organisms, and subjected to different conditions and diets.

All three ways of performing experiments and analyses may provide valuable information to the knowledge of the health effects of soy intake of average people. However all three ways both have

advantages and disadvantages; *Human cohort studies* have the advantage that they can be performed on very large groups of people, providing good basis for statistical conclusions, and elements of the individual persons entire life history can be part of the analyses – the disadvantages include that e.g. the reports of self-chosen random food intakes may give a very “noisy” set of subcategories, making it difficult to pinpoint specific health effects to specific food subjects; *Human intervention experiments* have the advantage that they can be performed in such a way that specific amounts of a food source can be pinpointed to specific health effects, although human study objects seldom can be forced to eat completely uniform diets and perform all other aspects of life in a uniform manner – the disadvantages include that the studied groups often are relatively small and heterogeneous leaving room for less firm statistical conclusions, that the time span of the experiment often is relatively short, and that humans cannot be subjected to deliberate overdoses of substances – *Laboratory animal experiments* have the advantage that animals can be specifically designed/bred to be very uniform and to have predispositions for specific diseases and anomalies e.g. cancer, gout, obesity, etc. Furthermore animal experiments are not subject to as strict ethical restrictions as human experiments. This allows the researchers to design experiments in which the toxicological effects of specific elements are tested on specific diseases or disorders. The results can easily be reproduced and offers a high degree of statistical validity, and the applied doses can be set so high that specific responses can be provoked out. The disadvantages of using laboratory animals includes that no animals are sufficiently similar to humans to exactly simulate human responses to particular elements or compounds. Furthermore the lives of humans are much more complex than the lives of laboratory animals in terms of external influences and complex diets, and thus important complex interactions and cross-reactions may be missed and disregarded.

*Human cohort experiment are the best to illustrate the response of average consumers, human intervention experiments are good at estimating the responses on a more specific level, and animal experiments are good at provoking both beneficial and detrimental effects, which sometimes are comparable to human effects.*

## **6.2. Effect of soy on the composition of cholesterol in humans**

*Intake of soy products has a documented positive effect on the composition of cholesterol types in the human body.*

It is a well-documented fact that the risk of e.g. cardio-vascular diseases is closely linked to the composition and amount of cholesterol in the body (EFSA, 2011). Cholesterols are lipids, and act as a precursor for the biosynthesis of steroid hormones, bile acids, and vitamin D, and are an important part of cell membranes in all parts of the body. Cholesterol is insoluble in the blood, but is readily transported in the blood when conjugated to different types of lipoproteins. In connection to health issues, the cholesterols are roughly divided into the “good” cholesterol, HDL (High Density Lipoprotein) and “bad” cholesterol, LDL (Low Density Lipoproteins). High levels of LDL are significantly associated with cardio-vascular diseases. Cholesterol is both synthesized in the body and is supplied with ingested foods.

A long line of investigations (e.g. Hermansen et al., 2003 and 2005; EFSA, 2011) have shown that intake of soy lowers the amount of LDL, whereas the concentration of HDL remains unchanged. The mechanisms of action remain uncertain and are probably linked to several components of the soy beans. However, it seems certain that soy proteins and their abilities to bind to cholesterol, and the resulting molecules cause the primary effects. Parallel to this, isoflavones and sterols have positive effects on the metabolism of fatty acids and cholesterol in the body, and fibre content has metabolism stimulating effects.

The American Food and Drug Administration (FDA) in 1999 performed (and verified in 2013) a thorough revision of the existing knowledge and experiments on cholesterol and soy proteins (FDA, 2013). FDA concluded that it is scientifically demonstrated that intake of soy proteins together with a diet of few saturated fatty acids has a lowering effect on LDL cholesterol, and stated that a daily intake of minimum 25g of soy protein significantly reduces the risk of cardiovascular diseases (FDA, 2013). A similar statement has been issued by the British Health authorities (JHCI) in 2002. Following a so called "Health Claim Application" a long list of EU's most prominent researchers were asked to evaluate whether it, from the existing evidence, is possible to claim that soy intake has a lowering effect on LDL cholesterol, and thereby has a health promoting effect. In a very strict scientific compilation of the very heterogeneous existing scientific evidence, it was assessed that evidence definitely pointed in the direction of a positive effect, but that the evidence was too heterogeneous and incomparable to conclude that there exists an unambiguous connection between a reduced risk of cardiovascular diseases and intake of soy proteins (EFSA, 2011). However, in any case, completely or partially reducing the intake of animal derived proteins and replacing these with soy proteins will have positive effects on the cholesterol composition of the body to, as many animal derived proteins have decidedly increasing effects on the levels of LDL cholesterol.

*Particularly fat reduced soy products, such as Soy4you® and Soy4you øko® have a positive effect on the cholesterol composition of the human body.*

### **6.3. Effect of soy on breast cancer**

*Human experiments show marginally positive effects in preventing and treating breast cancer with soy.*

Oestrogen is believed to play a central role in breast cancer development and progression. Blocking the effect of oestrogen, either by inhibiting oestrogen action or by reducing oestrogen production, has been widely used in breast cancer treatment, and soy isoflavones have shown to exert such effects (Shu et al., 2009). Isoflavones from soy have further been shown to have other anticancer effects, including the inhibition of DNA topoisomerase I and II, proteases, tyrosine kinases, inositol phosphate, and angiogenesis and may also boost immune responses (Shu et al., 2009). Consumption of soy food has, however, also been related to increasing the risk of breast cancer in some epidemiological studies (Trock et al., 2006), as genistein has been shown to enhance the proliferation of breast cancer cells *in vitro* and to promote oestrogen-dependent mammary tumour

growth in ovariectomized rats (Trock et al., 2006). In addition, breast cancer treatments may lead to a decrease in the endogenous estrogen supply of survivors, and a concern has been raised as to whether soy isoflavones may exert their estrogenic effects, promote cancer recurrence, and, thus, negatively influence overall survival.

In a large study, approximately 200.000 people of many ethnic lineages (Multi-ethnic Cohort Study) were followed for many years, and their diets and history of diseases were meticulously registered and analysed for a multitude of correlations (Conroy et al., 2013). Of these, 3841 persons were selected, because they were more than 50 years old and were diagnosed with breast cancer during the registration period. The conclusion of the analyses, including all ethnic groups, was that the amount of soy neither had a significant effect on the breast cancer related death frequency nor the duration of the courses of disease. However, within individual ethnic groups, significant positive effects on the duration of the courses of disease were registered (Conroy et al., 2013). This is in line with 5 smaller studies on American and Chinese Population groups (Boyapati et al., 2005; Fink et al., 2007; Guha et al., 2009; Shu et al., 2009; Caan et al., 2011), which all showed significantly slower development of breast cancer. In conclusion, statistically, it has not been established that intake of soy has a direct influence on the diagnosing of breast cancer, but that intake of soy very likely has a positive influence on the course of the disease.

*A large proportion of the isoflavones have been removed from Soy4you®, while a larger proportion remains in Soy4you øko®.*

#### **6.4 Effect of soy on prostate cancer**

*Human experiments show marginally positive effects in preventing and treating prostate cancer with soy.*

The components of soy primarily thought to suppress cancer are the soy isoflavones daidzein, genistein, and glycitein. Isoflavones accumulate in the prostate gland and have been shown to modulate endogenous hormones relevant to prostate carcinogenesis (Gardner et al., 2009). Soy isoflavones also exert nonhormonal effects to suppress cancer by altering expression of genes associated with cancer progression, and through pathways that target cell cycle and apoptosis in androgen prostate cancer cells (Handayani et al., 2006; Hamilton-Reeves et al., 2008 and 2013). However, a compilation of multiple human cohort studies, including groups of many ethnic origins and many types and frequencies of soy intake, showed that significant positive effects are relatively rare, and that most studies only show marginally positive effects (Ahmad et al., 2013; Perabo et al., 2008)).

*A large proportion of the bioactive isoflavones have been removed from Soy4you®, while a larger proportion remains in Soy4you øko®.*

## 6.5. Effect of soy on women's menopause

*Positive effects of soy intake on discomforts associated with the menopause of women are among the best documented in the catalogue of soy effects on human health*

In connection to the menopause the ovaries stops producing oestrogen, and this affects the tissue of the body and bodily functions in several ways. Many women experience hot flashes, heart palpitations, dry vaginal mucous membranes, and eventually an increased rate of bone fractures. Isoflavones from soybeans and other oestrogen-like phytoestrogens from e.g. soy and red clover have for many generations been used by women against discomforts caused by the menopause, and modern scientific investigations have demonstrated that the effects are scientifically significant.

*Osteoporosis* Human bones are not just dead calcareous elements providing structure to the body, but contain living cells which continuously build and degrade bone tissues, e.g. making the healing of bone fractures possible. The balance between the activity of the bone-degrading and -building cells is controlled by many different factors including the concentration of oestrogen in the blood. Therefore this balance can be affected by the consumption of phytoestrogen from soy, primarily inhibiting the activity of the bone degrading cells.

A large number of scientific investigations (EFSA, 2012), both on large and small population groups, show result which are ranging from significant to no effects of intake of isoflavones on the bone status and associated biological markers during and after the onset of menopause. Within many of the experiments, the results are relatively heterogeneous, which probably largely can be ascribed to the fact that many other factors, such as smoking and exercise, has a strong influence on the status of human bones. Investigations have demonstrated a dose-response dependent effect, and demonstrate that isoflavones only has an effect on the bone degradation if the persons also consume sufficient amounts of calcium in the diet (Kuhnle et al., 2011). As some soy products have a temporary tendency to decrease the absorption of calcium and other minerals, this emphasises the importance of consuming soy as part of a varied diet.

The effect of soy on other menopause related discomforts, such as hot flashes, heart palpitations and dry vaginal mucous membranes have similarly been demonstrated in a large number of scientific investigations (EFSA, 2012). The discomfort symptoms can be relatively difficult to quantify, as they are based on subjective evaluations of the involved, and there is no scientific consensus of the mechanisms of action of the isoflavones on the symptoms (Andrikoula et al., 2009). The results are ranging between clearly perceptible to no effects. A positive result is presented by Bolaños-Diaz et al., (2011), who in a comparison between medical hormone treatments and treatments with isoflavones, demonstrate that both groups had positive effect on life quality parameters, as compared to women receiving no treatments. Combining the medical and isoflavones treatments had no additional effect (Bolaños-Diaz et al., 2011). Other researchers (Reed et al., 2013; Amato et al., 2012; Burke et al., 2003) claim that effects of soy on the life quality of women in menopause is mainly due to placebo effects and differences in ethnic origin and the thereby accompanying differences in their diets during life.



In a so called "Health claim application", a selection of scientists from EU were asked to evaluate if it from the existing scientific knowledge can be claimed that isoflavones unambiguously affects the bone status and relieves symptoms of the menopause. Their conclusion was that a substantial amount of evidence points in the right direction, but that the evidences remain too in-comparable and fragmented, and that no unambiguous cause-effect has been established between isoflavones and the bone status and other menopause related discomforts. The American Drug and Food Administration (FDA) on the other hand, have established a connection between intake of soy and discomforts of menopause, and recommend a frequent intake of soy to relieve discomforts (Welty et al., 2007).

*A large proportion of the bioactive isoflavones have been removed from Soy4you®, while a larger proportion remains in Soy4you øko®.*

## 6.6. Soy and human reproduction

*No scientific investigations have shown detrimental effects of a moderate intake of soy on niether men's or women's fertility. A moderate soy intake of soy has not been shown to affect children in the foetal or infant stages, however pregnant women should not exaggerate the intake of soy.*

Even though isoflavones and other phytoestrogens in many ways resemble the humanly produced oestrogen, they have different modes of action in the human body. For example genestein has a 30 times poorer binding ability to one of oestrogens binding sites, ER $\beta$ , as compared to the other, ER $\alpha$  (Cederroth et al., 2012). ER $\beta$  is the primary binding site in the male prostate gland, which produces the majority of the seminal fluid and controls a large part of the male reproductive abilities, and it thus to be expected that the isoflavones have a relatively smaller effect on male reproduction as compared to female (Matthews et al., 2003). The number of scientific investigations evaluating the effect of phytoestrogens on the reproduction of men is limited, but no results points in the direction of neither a promoting nor a detrimental effect on the reproduction of men (Cederroth et al., 2012). A number of investigations on rats and mice indicate that a life-long excessive intake has a negative effect on the sexual development and fertility in males (Cederroth et al., 2012).

In women, the effect of the intake of isoflavones on the reproductive ability is more weel documented (Cederroth et al., 2012), and in a compilation of all the known investigations (Hooper et al., 2009) the connection between soy intake and different sexually related hormones and factors in fertile women was evaluated. The results showed that intake of isoflavones does not directly influence the natural oestrogen levels in the human body, but can have weak effects on some of the hormones which are associated with the menstrual cycle, and that intake of soy can be coupled to weakly prolonged menstrual periods. The results showed neither an increased nor a decreased ability to become pregnant or higher frequency of miscarriages or abnormal birth events.

Toxicological animal experiments on mice and rats have shown that exposure to large amounts of phytoestrogens can provoke different physiological changes in the reproductive organs (e.g. Gallo et al., 1999; Lamartiniere et al., 1998; You et al., 2002). Among farmers a well-known concept is "clover disease", where pregnant grassing animals almost exclusively feeding on highly



phytoestrogen rich clover will have an increased frequency of problems with pregnancies, and that the male offspring often will have a poorer fertility. So pregnant women should probably not base their diet exclusively on isoflavone-rich products, but let soy be part of a varied diet.

The foetal and infant stages are critical for the development of multiple physical traits in a human being. Particularly the sexual development is delicate, and concerns have been raised about the inclusion of phytoestrogens in the diet of pregnant women, breast feeding women and infants. A critical review of the existing publications reveals no reason for concern, as the results do not show any increased frequencies of abnormalities at moderate intakes of soy. An investigation of relatively high intakes of soy by a vegetarian group of women showed a slightly elevated frequency of abnormalities in new-born boys, however, the cases were also linked to cases of fly in the early pregnancy and to deficit iron levels in the diet of the inflicted women (North et al., 2000). Isoflavones are only very sparsely transmitted to the breast milk (Badger et al., 2009), so breast feeding women can safely include soy as part of a varied diet.

Soy product have a number of nutritional qualities, which makes them valuable as ingredients in infant formulas, and soy has for more than 40 years routinely been used for infants in large part of the Western world (Badger et al., 2009). In girls, a large number of studies of the effect of soy in infant formulas collectively show very few or no side effects or changes in e.g. the onset of puberty or other reproductive characteristics, however some studies showed a weakly increased risk of longer menstrual periods and menstrual pains (Strom et al., 2001), and for uterine fibroids in adult women who consumed soy as infants (D'Alosio et al., 2010). In boys, research show no or very moderate side effects in e.g. the onset of puberty and other reproductive traits (Cederroth et al., 2012). A long line of animal experiments collectively show very few tendencies of changed patterns of sexual development and life course as a consequence of soy intake (Cederroth et al., 2012).

*A large proportion of the isoflavones have been removed from Soy4you®, while a larger proportion remains in Soy4you øko®.*

## **6.7. Soy and mineral uptake**

*Scientific investigations show that balancing the intake of soy with other food sources eliminates the risk of mineral deficits.*

Soybeans and long line of other plant based food items contains phytates and oxylates, which are indigestible in the human organism, and reduces the uptake of important minerals such as calcium, iron, magnesium and zinc by producing insoluble chelates. Heat treatment of soy products, such as the products of Soy4you will dramatically reduce the content of phytates and oxylates.

Investigations have shown that any reductions in mineral uptake during soy intake is of a very temporary nature, and that consumption of other mineral rich food items quickly will compensate for the deficits (Jovaní et al., 2001). It is thus important to give the body frequent breaks in the soy intake so a healthy mineral balance can be maintained.

*The heat treatment of Soy4you® and Soy4you øko® dramatically reduces the content of phytates and oxylates, which potentially disturbs mineral uptake in the human intestine.*

## **6.8. Soy and allergies**

*The products of Soy4you are heat treated at relatively high temperatures, which causes a deactivation of a large proportion of the allergy causing proteins*

In Denmark, soy allergy is not particularly widespread (less than 0.7% in adults and 1.4% in small children (Sicherer, 2011)), and in small children, the prognosis of outgrowing the allergy is quite good. However food allergies are a serious problem, and people should be aware of their bodily responses to ingested food items. Soy beans is a legume, and some people experiencing allergic symptoms towards soy proteins will also experience allergic symptoms towards other legumes, e.g. green peas, lentils or peanuts. The reason for this is that the proteins in the legume food items are molecularly similar, and that the body cannot distinguish between the different allergy causing compounds. It is called a cross-reaction, however not all people allergic to soy will experience this. The only certain way to establish the allergy causing agents is a provoked test by a medical doctor.

Raw soy beans contain approximately 33 proteins, which potentially are allergenic (Amnuaycheewa, 2010). The proteins cause potential allergic reactions because they resemble the human body's own immunoglobulin E antibodies, which bind to receptors on mast cells and cause the allergic reaction. Heat and pressure treatment alters the shape of many proteins and dramatically reduce the allergenic potential of the proteins.

*Heat and pressure treated soy products, such as Soy4you® and Soy4you øko reduces the risk of evolving allergic reactions towards soy proteins*

## **6.9. Metabolism related issues of soy intake**

*Isoflavones may have negative on the metabolism of people with disorders in the thyroid balance. Soy4you® and Soy4you øko contain low levels of isoflavones*

Soybeans also contain moderate amounts of purine, which also is present in almost all food items. Consuming large amounts of purines can make gout worse, and persons with gout should not eat a lot of purine rich products. Moderate intake of purine-rich vegetables or protein is not associated with an increased risk of gout (Hyon et al., 2004)

Goitrogens are substances that suppress the function of the thyroid gland by interfering with iodine uptake, which can, as a result, cause an enlargement of the thyroid, i.e., a goiter. In *in vitro* studies and in rats, isoflavones have been shown to compete for an enzyme that is used to make thyroid hormone and partially inactivate thyroid peroxidase, an enzyme required for the synthesis of thyroid hormones. However, not only is the rat extremely sensitive to goitrogenic problems in comparison to humans, but despite inhibiting enzyme activity, soy-containing diets allow normal thyroid function. Soy may somewhat inhibit the absorption of synthetic thyroid hormone, such as synthroid, which is taken by hypothyroid patients. However, foods in general have this effect, as do fibre-rich

foods, herbs and many drugs. For this reason, thyroid hormone is taken on an empty stomach and hypothyroid patients can still consume soy products. If there is any small effect on absorption, the medication dose can easily be adjusted accordingly. There are however, two relevant clinical situations related to soy and thyroid function yet to be evaluated. One involves individuals with subclinical hypothyroidism, which represents about five per cent of the general adult population but a higher percentage among individuals over the age of 60. Patients with this condition have normal levels of the two primary thyroid hormones, thyroxine and triiodothyronine, but elevated levels of thyroid stimulating hormone. There is no direct evidence that soy pose a problem for subclinical hypothyroid patients and research specifically addressing this issue is currently underway. The second situation involves individuals whose iodine intake is marginal or inadequate. Some subpopulations may not be consuming sufficient iodine, such as women of reproductive age and vegetarians, and especially vegans, who do not use iodized salt, may be at increased risk of developing iodine deficiency. Consequently, vegans need to be especially mindful of their iodine intake, especially because they are often high-soy consumers (Messina, 2011). Research on humans indicates that you need not avoid soy if you experience hypothyroidism, as long as you are getting iodine either in your diet or through a supplement.

## **7. Properties of soy proteins in relation to different population segments**

*Isolated soy proteins are intermediary fast proteins, which favour both the building of muscles and the maintenance of other bodily functions*

The motivation for consuming soy proteins strongly depends on the needs and desires of the individual consumer. Some eat soy proteins to benefit from the many health promoting and disease preventing properties of soy. Others eat soy to build or reconstitute muscle tissue after sports or training. Some use soy proteins to gain or lose weight after disease, malnutrition, loss of appetite or obesity. Others eat soy because of religious or ethical considerations. Some eat soy to evade allergies towards other food sources. And finally, some eat soy simply because they find the taste appealing and like to occasionally substitute other protein sources with soy protein.

*Bodybuilders and sportsmen* In order to deliver peak performances or reduce the fat percentage in the body, many bodybuilders and sportsmen live by strictly controlled diet patterns, and many utilize protein powders as the main source of proteins. The primary origins of the proteins are from milk-whey or -casein, egg, meat or soybeans. Many investigations have evaluated the difference in efficiency of the different protein types on particularly stimulating the “Muscle Protein Synthesis” (MPS) after exercise (e.g. Tang et al., 2009; Diebert et al., 2001; Reidy et al., 2012). The overall conclusion of the investigations is that the speed of digestion and amino acid absorption, and the amino acid composition of the protein sources play a major role on the resulting muscle assimilation. “Fast” proteins, such as milk-whey are slightly superior in promoting synthesis of skeletal musculature, but inferior in overall protein assimilation in the rest of the body. “Slow” proteins, such as meat- and egg-proteins favour the overall protein assimilation over muscle assimilation. “Intermediary” fast proteins, such as milk-casein and isolated soy proteins favour

both the building of skeletal muscles and the maintenance of important organs such as intestines, liver and skin (Reidy et al., 2012; Yang et al., 2012; Deibert et al., 2011).

*Weight gainers* Some people have an acute need of gaining weight or maintaining a sufficient blood level of amino acids, but lack appetite or motivation to eat. These include anorectics, weak elderly people, hospitalized people, chemo patients, malnourished children, people with dysfunctional digestion or metabolism, etc. For many of these groups the lack of appetite or efficiency of amino acid uptake means that the ingested does not meet the demand of the body, and it is thus important to get a good “value for money” of the little food, which is actually ingested. Compared to fat and carbohydrates, proteins have a tendency of inducing a feeling of satiety and lack of appetite for more food (König et al., 2012; Lang et al., 1998; Veldhorst et al., 2009; Alfenas et al., 2010). For this purpose isolated “intermediary fast” proteins, such as soy proteins will serve as a concentrated source for complete protein. For hospitalized elderly patients the risk of secondary complications is high, and a study comparing the use of casein and soy as enteral protein sources concluded that soy proteins significantly reduced the risk of ulcers, intestinal complications and death as compared to casein (Espín et al., 2010). Soy protein has a high content of the amino acid leucine, which has proved to be a significant factor in the muscle building and weight gain of recovering cancer patients (Deutz et al., 2011).

*Weight loser* Obesity is a problem to an increasing number of people. Eating fat reduced, fibre-rich products, such as isolated soy proteins have the obvious advantage that the fat intake is reduced, as compared to e.g. meat. Soy proteins have been shown to induce the feeling of satiety faster than other protein sources such as casein and whey, thus reducing the further food intake (Alfenas et al., 2010). The rise in glycemic and insulinemic load gives good indications of the speed by which the blood sugar rises after the ingestion of a meal. A too fast rise in the loads of the blood will increase the risk of energy being allocated to storage (e.g. fat) rather than metabolic processes, resulting in a possible weight gain. Breakfast containing isolated soy proteins in comparison with a standard breakfast has been demonstrated to result in a significantly lower glycemic load (König et al., 2012).

*Vegetarians* Vegetarians and vegans have chosen to primarily base their food intake on plant derived food. This presents a challenge of obtaining all the necessary amino acids in adequate amounts, as some amino acids are relatively rare in plants. Isolated soy protein is a “complete protein” and thus provides all the essential amino acids. However, some soy products do also present certain challenges, as e.g. the phytic acid content may interfere with the uptake of minerals. Isolated soy proteins contain a very small amount of phytic acid and a normal mineral uptake is thus easily maintained (Mesina and Mesina, 2010).

*People with diseases or disorders* Although the established medicinal community is reluctant to recognize the intake of soy as the potential cure and prevention for a wide range of diseases and disorders, a growing number of people consume different soy products for medicinal or prophylactic purposes. Some disorders including hypocholesterol, menopause discomforts,

osteoporosis and coronary diseases have been recognised by particularly the American authorities to be decreased by the intake of soy (See also “Health aspects of soy consumption”).

*“Normal” people* People from East Asia have consumed soy products as part of their staple diet for millennia, and for the past decades people of the rest of the world have gradually increased the intake of soy. A large quantity of the consumed soy is consumed as a “hidden” ingredient in industrially produced food products, infant formulas, etc., but a growing proportion is also consumed because consumers deliberately chose soy over other protein products. Soy may not be the “miracle food” which some American agitators wish us to believe, but it is undeniable that isolated soy protein is a healthy, fat free source of complete protein, which, in many dishes, can replace meat.

*Isolated soy protein is a complete protein, and can serve as a healthy primary source of protein for most people.*

## **8. Environmentally sustainable proteins from soy**

*The production of soy protein has a smaller impact on the environment than animal proteins*

Increasing utilisation of plant protein is required to support the production of protein-rich foods that can replace animal proteins in the human diet to reduce the strain that intensive animal husbandry poses to the environment. From a nutritional standpoint, with the right combination, plant proteins can supply sufficient amounts of essential amino acids for human health requirements. Land plants have always been part of the human diet to provide energy and nutrients for sustainable living. Although plant proteins are relatively cheap and more abundant than animal proteins, direct consumption of proteins from land plants in conventional human food is still fairly limited. Currently, most plant proteins are used as animal feed to produce functional animal proteins from milk, eggs and meat (Day, 2013). However, the conversion of plant proteins into animal proteins is relatively inefficient. In some cases, less than 15% of the plant proteins from feed crops are turned into animal proteins for human consumption and 85% are wasted (Aiking, 2011; Pimentel & Pimentel, 2003). As a consequence, meat production is responsible for a disproportionate share of food-related environmental pressure (de Boer and Aiking, 2011; Gilland, 2002). With respect to land use, if the same amount of plant proteins is used directly for human consumption, less than 10% of land will be required to grow food crops as to otherwise feed crops to produce the same amount of meat proteins (de Boer and Aiking, 2011). Furthermore, production of animal proteins requires about 100 times more water than producing an equal amount of plant proteins (Pimentel & Pimentel, 2003). With the rapid growth in the world's population, food security has been seen as the next large challenge for the agrifood industry. Better and more efficient utilisation of plant-based proteins will become critical when the supply of animal proteins reaches maximum production capacity to feed the growing world population. The shift towards a more sustainable diet necessitates less reliance on foods of animal origin, and thus presents an huge potential for the agrifood industry to explore alternative sources of proteins (Aiking, 2011). For example, the development of new meat analogue products has accelerated in recent years, with some of the most

promising alternatives based on proteins from plant sources, such as soybean and peas, and the dairy substitutes market has also expanded. Plant protein-based meat and dairy substitutes can deliver equivalent quality at lower costs, while fulfilling the world's priority of reducing greenhouse gas emissions and limiting destruction of forest land (Dijkstra et al., 2003; Linnemann and Dijkstra, 2002). In addition, the right combination of plant proteins can ensure the supply of sufficient amounts of essential amino acids for human health requirements.

Soybean is one of the most important agricultural commodities because of its high protein content which is about 35–40%. Soybean is the dominant oil seed crop worldwide and the second largest source of vegetable oil, after palm oil. Currently, global production is estimated to be about 271 million metric tons per annum (Day, 2013), and a large amount of defatted soybean meal is produced after extraction of oil. Most defatted soybean meal is used for animal feed. A small portion is further processed into various types of soy protein products for human consumption. Although traditional foods made from soybean have been consumed throughout East Asia for more than two thousand years, in Western countries, soybean derived products have only become an economical and high quality vegetable protein source for human diets over the last few decades. Soy's high protein level and well-balanced amino-acid composition makes it an important source of plant protein, with a great potential to replace meat and dairy proteins in our daily diet (Day, 2013).

*Soy4you® and Soy4you øko® is produced in such a way that they can replace meat in many daily dishes*



## 9. References

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