

Request for Reconsideration after Final Action

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LAW OFFICE ASSIGNED	LAW OFFICE 105
MARK SECTION	
MARK FILE NAME	http://tmng-al.uspto.gov/resting2/api/img/85223292/large
LITERAL ELEMENT	LINKAGE CONNECTING RESOURCES FOR THE AGING
STANDARD CHARACTERS	NO
USPTO-GENERATED IMAGE	NO
ARGUMENT(S)	
Please see the actual argument text attached within the Evidence section.	
EVIDENCE SECTION	
EVIDENCE FILE NAME(S)	
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DESCRIPTION OF EVIDENCE FILE	Argument and Exhibits Thereto
GOODS AND/OR SERVICES SECTION (current)	
INTERNATIONAL CLASS	035
DESCRIPTION	
Providing services, namely group purchasing and consulting services to senior living and home care providers in the field of daily operations	

management for senior living facilities; providing daily operations management consulting, market demographic research and investment services relating to senior living organizations that serve an aging population	
FILING BASIS	Section 1(b)
GOODS AND/OR SERVICES SECTION (proposed)	
INTERNATIONAL CLASS	035
TRACKED TEXT DESCRIPTION	
<p>Providing services, namely group purchasing and consulting services to senior living and home care providers in the field of daily operations management for senior living facilities; Providing services, namely, distributorship services featuring food, medical supplies, office products, pharmacy products, paint and painting supplies, and personal emergency response systems, all for senior living organizations that serve the aging population both on and off of their senior living campuses; providing daily operations management consulting, market demographic research and investment services relating to senior living organizations that serve an aging population; providing business management services, namely, providing business operations management services to senior living organizations that serve the aging population both on and off of their senior living campuses; providing energy conservation services, namely, providing consulting services in the fields of energy consumption and usage to improve energy efficiency, all for senior living organizations that serve the aging population both on and off of their senior living campuses</p>	
FINAL DESCRIPTION	
<p>Providing services, namely, distributorship services featuring food, medical supplies, office products, pharmacy products, paint and painting supplies, and personal emergency response systems, all for senior living organizations that serve the aging population both on and off of their senior living campuses; providing business management services, namely, providing business operations management services to senior living organizations that serve the aging population both on and off of their senior living campuses; providing energy conservation services, namely, providing consulting services in the fields of energy consumption and usage to improve energy efficiency, all for senior living organizations that serve the aging population both on and off of their senior living campuses</p>	
FILING BASIS	Section 1(b)
SIGNATURE SECTION	
RESPONSE SIGNATURE	/april l besl/
SIGNATORY'S NAME	April L Besl
SIGNATORY'S POSITION	Attorney of record, Ohio bar member
SIGNATORY'S PHONE NUMBER	5139778527
DATE SIGNED	02/18/2016
AUTHORIZED SIGNATORY	YES
CONCURRENT APPEAL NOTICE FILED	YES
FILING INFORMATION SECTION	
SUBMIT DATE	Thu Feb 18 10:06:48 EST 2016
TEAS STAMP	USPTO/RFR-XX.XXX.XX.XX-20 160218100648377068-852232 92-5507fbe1417412413b1179 d40c9bcc51c8e7dd64fb0f2a2 e4dbfde079661ba9b0ef-N/A- N/A-20160218100030134472

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OMB No. 0651-0050 (Exp 07/31/2017)

Request for Reconsideration after Final Action

To the Commissioner for Trademarks:

Application serial no. **85223292** LINK·AGE CONNECTING RESOURCES FOR THE AGING (Stylized and/or with Design, see <http://tmng-al.uspto.gov/resting2/api/img/85223292/large>) has been amended as follows:

ARGUMENT(S)

In response to the substantive refusal(s), please note the following:

Please see the actual argument text attached within the Evidence section.

EVIDENCE

Evidence in the nature of Argument and Exhibits Thereto has been attached.

JPG file(s):

[Evidence-1](#)

[Evidence-2](#)

[Evidence-3](#)

[Evidence-4](#)

[Evidence-5](#)

[Evidence-6](#)

[Evidence-7](#)

Original PDF file:

[evi_661926435-20160218100030134472_ .eration - LINKAGE_CONNECTING_RESOURCE_FOR_THE_AGING_Design.pdf](#)

Converted PDF file(s) (27 pages)

[Evidence-1](#)

[Evidence-2](#)

[Evidence-3](#)

[Evidence-4](#)

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[Evidence-7](#)

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[Evidence-27](#)

Original PDF file:

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Converted PDF file(s) (2 pages)

[Evidence-1](#)

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Converted PDF file(s) (9 pages)

[Evidence-1](#)

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Converted PDF file(s) (1 page)

[Evidence-1](#)

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[Evidence-1](#)

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[Evidence-10](#)

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[Evidence-1](#)

[Evidence-2](#)

[Evidence-3](#)

[Evidence-4](#)

[Evidence-5](#)

Original PDF file:

CLASSIFICATION AND LISTING OF GOODS/SERVICES

Applicant proposes to amend the following class of goods/services in the application:

Current: Class 035 for Providing services, namely group purchasing and consulting services to senior living and home care providers in the field of daily operations management for senior living facilities; providing daily operations management consulting, market demographic research and investment services relating to senior living organizations that serve an aging population

Original Filing Basis:

Filing Basis: Section 1(b), Intent to Use: For a trademark or service mark application: As of the application filing date, the applicant had a bona fide intention, and was entitled, to use the mark in commerce on or in connection with the identified goods/services in the application. **For a collective trademark, collective service mark, or collective membership mark application:** As of the application filing date, the applicant had a bona fide intention, and was entitled, to exercise legitimate control over the use of the mark in commerce by members on or in connection with the identified goods/services/collective membership organization. **For a certification mark application:** As of the application filing date, the applicant had a bona fide intention, and was entitled, to exercise legitimate control over the use of the mark in commerce by authorized users in connection with the identified goods/services, and the applicant will not engage in the production or marketing of the goods/services to which the mark is applied, except to advertise or promote recognition of the certification program or of the goods/services that meet the certification standards of the applicant.

Proposed:

Tracked Text Description: ~~Providing services, namely group purchasing and consulting services to senior living and home care providers in the field of daily operations management for senior living facilities;~~ Providing services, namely, distributorship services featuring food, medical supplies, office products, pharmacy products, paint and painting supplies, and personal emergency response systems, all for senior living organizations that serve the aging population both on and off of their senior living campuses; ~~providing daily operations management consulting, market demographic research and investment services relating to senior living organizations that serve an aging population;~~ providing business management services, namely, providing business operations management services to senior living organizations that serve the aging population both on and off of their senior living campuses; providing energy conservation services, namely, providing consulting services in the fields of energy consumption and usage to improve energy efficiency, all for senior living organizations that serve the aging population both on and off of their senior living campuses

Class 035 for Providing services, namely, distributorship services featuring food, medical supplies, office products, pharmacy products, paint and painting supplies, and personal emergency response systems, all for senior living organizations that serve the aging population both on and off of their senior living campuses; providing business management services, namely, providing business operations management services to senior living organizations that serve the aging population both on and off of their senior living campuses; providing energy conservation services, namely, providing consulting services in the fields of energy consumption and usage to improve energy efficiency, all for senior living organizations that serve the aging population both on and off of their senior living campuses

Filing Basis: Section 1(b), Intent to Use: For a trademark or service mark application: As of the application filing date, the applicant had a bona fide intention, and was entitled, to use the mark in commerce on or in connection with the identified goods/services in the application. **For a collective trademark, collective service mark, or collective membership mark application:** As of the application filing date, the applicant had a bona fide intention, and was entitled, to exercise legitimate control over the use of the mark in commerce by members on or in connection with the identified goods/services/collective membership organization. **For a certification mark application:** As of the application filing date, the applicant had a bona fide intention, and was entitled, to exercise legitimate control over the use of the mark in commerce by authorized users in connection with the identified goods/services, and the applicant will not engage in the production or marketing of the goods/services to which the mark is applied, except to advertise or promote recognition of the certification program or of the goods/services that meet the certification standards of the applicant.

SIGNATURE(S)

Request for Reconsideration Signature

Signature: /april l besl/ Date: 02/18/2016

Signatory's Name: April L Besl

Signatory's Position: Attorney of record, Ohio bar member

Signatory's Phone Number: 5139778527

The signatory has confirmed that he/she is an attorney who is a member in good standing of the bar of the highest court of a U.S. state, which includes the District of Columbia, Puerto Rico, and other federal territories and possessions; and he/she is currently the owner's/holder's attorney or an associate thereof; and to the best of his/her knowledge, if prior to his/her appointment another U.S. attorney or a Canadian attorney/agent not currently associated with his/her company/firm previously represented the owner/holder in this matter: (1) the owner/holder has filed or is concurrently filing a signed revocation of or substitute power of attorney with the USPTO; (2) the USPTO has granted the request of the prior representative to withdraw; (3) the owner/holder has filed a power of attorney appointing him/her in this matter; or (4) the owner's/holder's

appointed U.S. attorney or Canadian attorney/agent has filed a power of attorney appointing him/her as an associate attorney in this matter.

The applicant is filing a Notice of Appeal in conjunction with this Request for Reconsideration.

Serial Number: 85223292

Internet Transmission Date: Thu Feb 18 10:06:48 EST 2016

TEAS Stamp: USPTO/RFR-XX.XXX.XX.XX-20160218100648377

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT:	Senior Resource Alliance
SERIAL NO.:	85/223292
MARK:	LINK·AGE CONNECTING RESOURCES FOR THE AGING & Design
OFFICE ACTION MAILING DATE:	August 18, 2015
EXAMINING ATTORNEY:	Maureen Dall Lott Law Office 105

REQUEST FOR RECONSIDERATION

I. Introduction

In the August 18, 2015 Final Office Action, the Examining Attorney refused the amendment of Applicant's services under its LINK·AGE CONNECTING RESOURCES FOR THE AGING & Design mark to: "*Providing services, namely group purchasing and consulting services to senior living and home care providers in the field of daily operations management for senior living facilities; providing daily operations management consulting, market demographic research and investment services relating to senior living organizations that serve an aging population,*" in Class 35.

Instead, the Examining Attorney noted that Applicant may adopt the following identification of services, if accurate: "*Providing services, namely, distributorship services featuring food, medical supplies, office products, pharmacy products, paint and painting supplies, and personal emergency response systems, all for senior living organizations that serve the aging population both on and off of their senior living campuses; providing business management services, namely, providing business operations management services to senior living organizations that serve the aging population both on and off of their senior living campuses; providing energy conservation services, namely, providing consulting services in the fields of energy consumption and usage to improve energy efficiency, all for senior living*

organizations that serve the aging population both on and off of their senior living campuses,” in Class 35. Applicant hereby adopts the identification of services as suggested by the Examining Attorney, and has amended its application to that extent in connection with the filing of this reply.¹

The Examining Attorney also maintained the refusal of registration of Applicant’s LINK·AGE CONNECTING RESOURCES FOR THE AGING & Design trademark on the basis of a potential likelihood of confusion with registrations for five separate marks:

(1) LINKAGE (Reg. No. 2,463,209) for “*Business consulting services, relating to business and performance management, leadership, personnel recruitment and selection, career development, human resources business partnering, and designing rewards and recognition programs*” in Class 35 and “*Educational services, namely, conducting conferences, institutes, seminars, workshops, and classes in business and performance management, leadership, personnel recruitment and selection, career development, human resources business partnering, and designing rewards and recognition programs*” in Class 41;

(2) and (3) ASIAINFO LINKAGE and Designs (U.S. Reg. Nos. 4,425,909 and 4,425,910) for “*Computer software, namely, software for use in billing, account support and management, clearing and settlement of financial transactions, customer relationship management, partnership relationship management, automate data gathering and warehousing to manage transactional data, provide statistical analysis,*

¹ The identification of services suggested by the Examining Attorney is identical to the last identification of services that was accepted by the USPTO in connection with Applicant’s LINK·AGE trademark. The Examining Attorney’s August 18, 2015 Office Action Letter based its analysis on the accepted identification of services, and Applicant’s reply relies upon the same.

and produce notifications and reports, data mining, and security, namely, user authentication and controlling computer network access, firewalls for preventing intrusion and hacking, mobile device management, e-mail; computer software platform for use in mobile e-commerce, namely, an electronic financial platform that accommodates multiple types of payment and debt transactions in an integrated mobile device and allow users to perform electronic business transactions via a global computer network; computer software platform for use in computer network management and analytics used for process management, operations, namely, for billing verification, fraud detection, monitoring, measuring, analyzing, security managing, network surveillance, signal classification, traffic managing, creating and monitoring call detailed records, fraud detection and reporting information extracted from networks, switches, operating systems, of mobile devices; computer software platform for use in advertising and marketing analysis, user traffic analysis, and customer segmentation and profiling; computer software platform for use in content delivery, namely, video on demand, music on demand, text on demand, audio on demand, streaming media, application map; computer software, namely, software development tools for network management and security” in Class 09 and “Providing business intelligence consulting services; outsourcing services in the field of customer relationship management” in Class 35;

(4) A-LINKAGE (Reg. No. 3,379,376) for *“Dietary Supplements sold as an integral component of Essential oils and cosmetics” in Class 03, “Dietary Supplements sold as an integral component of Vitamins, Mineral Supplements, Nutritional Supplements” in Class*

05, and “*Dietary Supplements sold as an integral component of fruit drinks and fruit juices and syrups for making teas and sports drinks*” in Class 32; and

(5) LINKAGE (Registration No. 4,533,656) for “*Agricultural seeds; Fresh corn; Fresh fruit and vegetables; Fresh potatoes; Herb seeds for planting; Plant seeds; Raw mushrooms; Raw oats; Raw potatoes; Seeds and bulbs; Seeds for agricultural purposes; Spores and spawn; Unprocessed corn; Unprocessed edible seeds; Unprocessed grain; Unprocessed oats; Unprocessed potatoes*” in Class 31.

The Examining Attorney maintains that Applicant’s LINK·AGE CONNECTING RESOURCES FOR THE AGING & Design mark is confusingly similar to the cited registrations because the marks share the words “LINKAGE” or “LINK AGE”, and because of an allegation that Applicant’s mark is used in connection with services that are related to the goods and services registered under the cited marks.

Applicant respectfully disagrees with the Examining Attorney’s finding of potential likelihood of confusion because: (i) Applicant’s mark is distinguishable in sight, sound, meaning and commercial impression; (ii) the goods and services are not so related as to be likely to cause confusion; (iii) Applicant’s channels of trade are distinct from those of the cited marks; (iv) the significant level of sophistication among the relevant consumers makes confusion particularly unlikely; and (v) the high level of coexistence among marks utilizing the cited terms indicates that the terms afford weak protection, and Applicant’s mark should also be allowed to coexist.

Applicant therefore respectfully requests that the Examiner reconsider the refusal. A Notice of Appeal of the Final Refusal is being filed simultaneously with the Trademark Trial and Appeal Board.

II. Applicant's Mark is Distinguishable in Sight, Sound, Meaning and Commercial Impression from the Cited Registrations when Considered as a Whole and Not Dissected.

When considering likelihood of confusion, “[a]ll relevant facts pertaining to appearance, sound, and connotation must be considered *before* similarity as to one or more of [the DuPont] factors may be sufficient to support a finding that the marks are similar or dissimilar.” *Recot, Inc. v. M.C. Becton*, 214 F.3d 1322, 1329, 54 USPQ2d 1894, 1899 (Fed. Cir. 2000) (emphasis added).

Moreover, it is a “basic principle in determining confusion between marks ...that marks must be *compared in their entirety* It follows from that principle that likelihood of confusion *cannot be predicated on dissection* of a mark, that is, on only part of a mark.” TMEP § 1207.01(b) (emphasis added). *In re Nat'l Data Corp.*, 753 F.2d 1056, 1058, 224 USPQ 749, 750-51 (Fed. Cir. 1985) (footnotes omitted) (citations omitted); *See In re Shell Oil Co.*, 992 F.2d 1204, 1206, 26 USPQ2d 1687, 1688 (Fed. Cir. 1993); *Massey Junior Coll., Inc. v. Fashion Inst. of Tech.*, 492 F.2d 1399, 1402, 181 USPQ 272, 273-74 (C.C.P.A. 1974).

Furthermore, the “meaning” of the marks must be considered in relation to the named goods or services. Even marks that are identical in sound and/or appearance may create sufficiently different commercial impressions when applied to the respective parties’ goods or services so that there is no likelihood of confusion. *See, e.g., In re Sears, Roebuck & Co.*, 2 USPQ2d 1312, 1314 (TTAB 1987) (holding CROSS-OVER for bras and CROSSOVER for ladies’ sportswear not likely to cause confusion, noting that the term “CROSS-OVER” was suggestive of the construction of applicant’s bras, whereas “CROSSOVER,” as applied to

registrant's goods, was "likely to be perceived by purchasers either as an entirely arbitrary designation, or as being suggestive of sportswear which "crosses over" the line between informal and more formal wear... or the line between two seasons."); *In re British Bulldog, Lt.d*, 224 USPQ 854, 856 (TTAB 1984) (PLAYERS for men's underwear not likely to cause confusion with PLAYERS for shoes); *In re Sydel Lingerie Co.*, 197 USPQ 629, 630 (TTAB 1977) (BOTTOMS UP for ladies' and children's underwear not likely to cause confusion with BOTTOMS UP for men's clothing). Applicant has addressed each of the cited registrations in turn below.

A) Applicant's Mark is Not Confusingly Similar to LINKAGE (Reg. 2463209).

The Examining Attorney correctly explained that marks may be confusingly similar in appearance where similar terms or phrases appear in the compared marks and create a similar overall commercial impression. However, Applicant contends that the Examining Attorney erred by assuming that the commercial impression was identical.

It is well established under the "anti-dissection" rule that it is improper to allow one aspect of the similarity factor to supersede all other aspects. *Recot*, 214 F.3d at 1329. In *Recot*, for example, the Federal Circuit held that the TTAB erred by only considering the connotation or meaning of the marks, thus failing to give due consideration to sight, sound and commercial impression. *Id.* Here, Applicant believes that the Examining Attorney has placed undue weight on the sight aspect, and has not adequately considered meaning and commercial impression. This is precisely what happened in the above-cited case *In re Sears, Roebuck & Co.*, 2 USPQ2d at 1314.

Both Applicant's mark and the LINKAGE mark in Reg. 2463209 contain the same letters, but it is apparent that Applicant's mark functions as two words whereas the registered

mark only functions as one. In that context, the marks read differently and convey an entirely different meaning, particularly when considered in light of the services being offered. The word “linkage” is defined as either a state of being linked or connected, or a relationship connecting one thing to another. See Dictionary Definitions of Linkage attached hereto as **Exhibits A-B**.

As described in its identification of services, the LINKAGE mark in Reg. 2463209 is used in connection with various types of human resource management, such as recruitment, career development, leadership and “rewards and recognition programs.” In that context, the meaning of the registered mark suggests development and strengthening of the relationship or connection between employees and employers. By contrast, the word “link” means to connect and the word “age” means a period of human life, and may also carry a connotation of advanced years. See Dictionary Definitions of Link attached hereto as **Exhibits C-D**; Dictionary Definitions of Age attached hereto as **Exhibits E-F**. The services of Applicant’s mark are described as including distributorship and management that only benefits senior citizen communities. In other words, Applicant’s services suggest a “link” for people of elderly “age.”

In light of the foregoing, the analysis here is highly similar to those in the CROSS-OVER, PLAYERS, and BOTTOMS UP cases. In fact, each of those analyses should be considered closer cases than this one, because each involved applicants and registrants who were in the apparel business. Here, there is no question as to the fact that Reg. 2463209 and Applicant are not involved in the same type of business, even when taking into consideration the Examining Attorney’s argument that the services are broadly defined. Specifically, Reg. 2463209 is engaged in business consulting whereas the Applicant is engaged in business

management², and the natures of the relative consulting and management services, as defined in their identifications of services, diverge as explained further below. Furthermore, although Applicant notes that consulting services and management services are entirely different types of services, even in light of the Examining Attorney's prior contention that they are related, it must be acknowledged that the services are targeting different consumers and thus still create differing commercial impressions, such as in *Schwarzkopf v. John H. Breck, Inc.*, 52 C.C.P.A. 957, 959 (C.C.P.A. 1965). There, the Federal Circuit explained that shampoo targeting women created a different meaning and commercial impression from shampoo targeting children, despite the fact that both marks featured a female silhouette facing to the left. Here, the difference is more drastic, as consultants and managers do not share functions in the same way that two types of shampoo do.

In sum, Reg. 2463209 for LINKAGE creates the impression of consulting services that strengthen the bonds between employers and employees, while Applicant's mark creates the impression of management services that keep senior citizens connected, both inside and outside of their senior living communities. Thus, it should be apparent that Applicant's mark, as used in connection with its services, creates a completely different commercial impression than Reg. 2463209 and is not confusingly similar.

B) Applicant's Mark is Not Confusingly Similar to ASIAINFO LINKAGE (Reg. 4425909 and 4425910).

Similar to the above analysis, Applicant contends that the Examining Attorney has improperly dissected the marks in comparing ASIAINFO LINKAGE with LINK·AGE, by placing undue weight upon the "sight" aspect and excluding the term "ASIAINFO" from the

² Although Applicant's identification also includes a separate reference to consulting services "in the field of energy consumption," that service is narrowly defined and thus has no overlap with either Registration No. 2,463,209 or 4,425,909 and 4,425,910, as acknowledged in the Final Office Action's "PLEASE NOTE" section.

analysis. Although the Examining Attorney is correct that additional weight may be given to a dominant feature of a mark, the analysis in the Final Office Action did not adequately determine whether ASIAINFO or LINKAGE is the dominant feature of the registered mark, and ultimately gave no weight to ASIAINFO while explaining the sight, sound, meaning and commercial impression.

Although there is no mechanical test to select a “dominant” element of a compound word mark, consumers would be more likely to perceive a fanciful or arbitrary term, rather than a descriptive or generic term, as the source-indicating feature of the mark. *See, e.g., In re Dixie Rests., Inc.*, 105 F.3d 1405, 1407, 41 USPQ2d 1531, 1533-34 (Fed. Cir. 1997). In regard to Reg. 4425909 and 4425910, a review of the registered goods and services demonstrates that “linkage” is significantly more descriptive of those goods and services than “asiainfo.”

Although four International Classes are covered by the registered mark, none of the described goods and services make any mention of Asia or anything that relates to Asia. Likewise, the rather lengthy identification only uses the word “information” twice, and only in the context of analyzing information or transmitting information. The remainder of the identification of goods and services is filled with terms speaking directly to connection or linkage, such as “customer... partnership relationship management,” “controlling computer network access,” “mobile e-commerce,” “electronic business transactions via a global computer network,” “computer network management,” “computer software platform for use in advertising and marketing analysis,” “user traffic analysis,” “content delivery,” “outsourcing in the field of customer relationship management,” “telecommunications gateway services,” “integration of computer systems and networks,” and “internet access, internet protocol telephony, and virtual private networks.” The fact that ASIAINFO is the real dominant term for the registered mark is

further buttressed by the ownership of the marks by a company called “Asiainfo Holdings, Inc.” and that company’s simultaneous ownership of no less than five (5) other registered trademarks for ASIAINFO. See Registration Certificates attached hereto as **Exhibits G-K**.

In light of the foregoing, it was improper for the Examining Attorney to place greater weight on LINKAGE in this comparison of Applicant’s mark with Reg. 4425909 and 4425910. Greater weight should have been placed upon ASIAINFO instead, and in that context, it is quite clear that Reg. 4425909 and 4425910 are not similar enough in appearance or sound to Applicant’s mark to cause likelihood of confusion.

Additionally, similar to Applicant’s argument in section II(A), a comparison of the full marks here in connection with the goods and services being offered shows that there is a notable difference in meaning. Like above, Reg. 4425909 and 4425910 are registered in connection with business consulting services (*i.e.* “business intelligence consulting”), in addition to software and “software platforms,” whereas the cited section of Applicant’s identification lists business management and distributorship services. A careful reading of the goods and services for Reg. 4425909 and 4425910 demonstrates that the consulting services and the goods offered in connection therewith deal with computer networks, internet technology, communications technology, marketing and advertising, and billing/customer relations, including outsourcing. In that context, and giving all due weight to the dominant term ASIAINFO, Reg. 4425909 and 4425910 suggest a meaning of a company, called “Asiainfo,” that connects via internet and communications technology. The presence of the corporate design logo within the registered mark further accentuates the importance of ASIAINFO as the identifying feature in that analysis.

By contrast, the Applicant’s use of “link” and “age” in connection with business management and distributorship services to senior living communities does not, at all, implicate

ASIAINFO, nor does the identification of goods and services refer to consultation on internet or communications technology. Instead, Applicant's mark generally suggests a "link" for people of older "age." Furthermore, the presence of Applicant's corporate logo in its mark strengthens the distinction from the identifying feature of the registered mark.

Again, this comparison should result in the same outcome as that in the CROSS-OVER matter or the other similar citations. Here, the analysis is even more to Applicant's favor, since LINKAGE is not the dominant term for Reg. 4425909 and 4425910. Instead, ASIAINFO is the dominant term. In connection with sight, sound and meaning, Reg. 4425909 and 4425910 create a commercial impression of a company, "Asiainfo," identified with a distinct corporate logo that connects businesses and consumers via a wide range of internet technology and communications goods and consulting services. By contrast, Applicant's mark creates a commercial impression of a different company with a different corporate logo providing management and distributorship services to keep senior citizens connected, both inside and outside of their senior living communities. Thus, it should be apparent that Applicant's mark, as used in connection with its services, creates a completely different commercial impression than Reg. 4425909 and 4425910 and is not confusingly similar.

C) Applicant's Mark is Not Confusingly Similar to A-LINKAGE (Reg. 3379376).

Similar to the above analysis, Applicant contends that the Examining Attorney has again improperly dissected the marks in comparing A-LINKAGE in Reg. 3379376 with LINKAGE, by placing undue weight upon the "sight" aspect and excluding the term "A-" from the analysis. Although the Examining Attorney is correct that additional weight may be given to a dominant feature of a mark, the analysis in the Final Office Action did not properly determine the

dominant feature of the registered mark and gave no weight to A- while explaining the sight, sound, meaning and commercial impression.

Again, consumers are more likely to see a more descriptive term as not being the dominant term. *In re Dixie Rests., Inc.*, 105 F.3d at 1407. In regard to Reg. 3379376, a review of the registered goods and services and proper evaluation of terminology used in the industry or trade of dietary/nutritional supplement/components demonstrates that A- is a suggestive term loosely referring to an A-type proanthocyanidin, in which case LINKAGE is a descriptive term describing the chemical structure of an A-type proanthocyanidin and its ability to bond to proteins. As evidence, Applicant has attached information demonstrating that the types of dietary or nutritional supplement/components that Reg. 3379376 offers for sale include A-type proanthocyanidins present within its supplement/components, and information explaining the chemistry of “A-type linkage” in such proanthocyanidins. See Screenshots attached hereto as **Exhibits L-O**.

In light of the foregoing, it was improper for the Examining Attorney to place greater weight on LINKAGE in Reg. 3379376 for the analysis. Greater weight should have been placed on A- instead, and in that context, it is quite clear that Reg. 3379376 is not similar enough in appearance or sound to Applicant’s mark to cause likelihood of confusion.

Additionally, similar to Applicant’s argument in section II(A), a comparison of the full marks here in connection with the goods and services being offered shows that there is a notable difference in meaning. The registrant here has registered their mark in connection with the sale of certain dietary and nutritional supplement/components, whereas the cited section of Applicant’s identification lists distributorship services featuring food, medical supplies, and pharmacy products. A careful reading of the identification of goods for Reg. 3379376 and the

attached evidence explains the relationship between the "A-" term in registrant's mark and the dietary supplement/components being offered in connection therewith. Specifically, A-type proanthocyanidins are present in registrant's "CranSmart" cranberry extract, and the company claims that the "linkage" of A-type proanthocyanidins has the effect of preventing or otherwise inhibiting urinary tract infections. In that context, and giving all due weight to the dominant term A-, the registrant's mark suggests a meaning of a specific beneficial health effect related to a specific chemical structure.

By contrast, the Applicant's use of "link" and "age" in connection with distributorship services to senior living communities does not, at all, implicate a chemical structure or any effects associated therewith, nor does the identification of goods and services refer to the offering of supplements. Instead, Applicant's mark generally suggests a "link" for people of older "age." Although it is understood that the Examining Attorney posited that Applicant's identification could indirectly implicate supplements via food, medical supplies or pharmacy products, such an implication would only be in reference to distributorship services and not the manufacture of goods, and would still not create the same meaning as the registered mark, since Applicant's mark lacks the dominant A- term.

Again, this comparison should result in the same outcome as that in the CROSS-OVER matter. Here, the analysis is even more to Applicant's favor, since LINKAGE is not the dominant term for Reg. 3379376. Instead, A- is the dominant term. In connection with sight, sound and meaning, the registered mark creates a commercial impression of specific health benefits from a specific chemical structure that is present in the supplement/components sold by the registrant. By contrast, Applicant's mark creates a commercial impression of distributorship services to keep senior citizens connected, both inside and outside of their senior living

communities. Thus, it should be apparent that Applicant's mark, as used in connection with its services, creates a completely different commercial impression than Reg. 3379376 and is not confusingly similar.

D) Applicant's Mark is Not Confusingly Similar to LINKAGE (Reg. 4533656).

Similar to the above analysis, Applicant contends that the Examining Attorney has improperly dissected the marks in comparing LINKAGE with LINK·AGE, by placing undue weight upon the "sight" aspect, and has not adequately considered meaning and commercial impression.

Both Applicant's mark and Reg. 4533656 contain the same letters, but it is apparent that Applicant's mark functions as two words whereas the registered mark only functions as one. In that context, the marks read differently and convey an entirely different meaning, particularly when considered in light of the goods and services being offered. The word "linkage" is defined as either a state of being linked or connected, or a relationship connecting one thing to another. *See Exhibits A-B.* As described in its identification of services, the registered mark is used in connection with the sale of various types of seeds, agricultural products and fresh fruits and vegetables. In that context, the meaning of the registered mark suggests a connection to agriculture, horticulture, fruits or vegetables. By contrast, the word "link" means to connect and the word "age" means a period of human life, and may also carry a connotation of advanced years. *See Exhibits C-F.* The services of Applicant's mark are described as including distributorship of various supplies, including medical supplies, personal emergency response systems, and food that only benefit senior citizen communities. In other words, Applicant's services suggest a "link" for people of elderly "age."

In light of the foregoing, the analysis here is highly similar to those in the CROSS-OVER, PLAYERS, and BOTTOMS UP matters. In fact, each of those analyses should be considered closer cases than this one, because each involved applicants and registrants who were selling apparel. Here, there is no question as to the fact that Reg. 4533656 and Applicant are not involved in the same type of business, even when taking into consideration the Examining Attorney's argument that the goods and services are broadly defined and both include references to food. Specifically, Reg. 4533656 is engaged in the production and sale of very specific types of food, whereas Applicant does not produce any food, and instead only distributes various products, including food, to senior citizens.

In sum, Reg. 4533656 creates the impression of a producer of specific foodstuffs connecting people with agriculture, horticulture, and fresh fruits and vegetables, while Applicant's mark creates the impression of a distributor keeping senior citizens connected, both inside and outside of their senior living communities. Thus, it should be apparent that Applicant's mark, as used in connection with its services, creates a completely different commercial impression than the registered mark and is not confusingly similar.

III. The Goods and Services Are Not so Related as to be Likely to Cause Confusion

The Examining Attorney correctly noted that the goods and/or services of the parties need not be identical or even competitive to find a likelihood of confusion. *On-line Careline Inc. v. Am. Online Inc.*, 229 F.3d 1080, 1086 (Fed. Cir. 2000). However, this acknowledgement of the general rule allowing likelihood of confusion to be found in cases of merely related goods and services does not compel that this factor be found in favor of confusion whenever the goods and services are arguably related. In fact, both the TTAB and the Federal Circuit have explained that such analysis is erroneous, and "[e]ach case must be decided on its own facts and the differences are often subtle ones." *Jacobs v. Int'l Multifoods Corp.*, 668 F.2d 1234, 1236

(C.C.P.A. 1982)(citing *Industrial Nucleonics Corp. v. Hinde*, 475 F.2d 1197, 1199 (CCPA 1973)).

For example, despite there being some level of relatedness between restaurant services and food, the Federal Circuit has held that “something more” must be shown beyond a simple allegation that some restaurants sell the same types of food or drink as the goods at issue, and instead, there must be “substantial evidence” that the consuming public will believe that the goods and services emanate from the same source. *In re Coors Brewing Co.*, 343 F.3d 1340, 1346 (Fed. Cir. 2003). Similarly, the Board has noted that the ubiquitous nature of computer hardware and software in the modern world means that the fact that two parties provide “computer software” is insufficient to establish relatedness, absent specific proof that consumers are likely to believe that the type of software in question emanates from the same source. *Electronic Data Systems Corporation v. EDSA Micro Corporation*, 23 U.S.P.Q.2D (BNA) 1460, 1463 (TTAB 1992).

Here, the Examining Attorney has held that: (i) business consulting services and business management services are related; (ii) distributorship of office products and production of computer software are related; (iii) distributorship of food, medical supplies and pharmacy products and production of dietary/nutritional supplement/components are related; and (iv) distributorship of food and production of various agricultural, fruit and vegetable products are related. Applicant asserts that these goods and services are not so related as to be likely to cause confusion, particularly in light of the precedent cited above.

A) Registrants' Business Consulting/Software Goods and Services and Applicant's Business Management and Distributorship Services Are Not Related.

The Examining Attorney has alleged that the broad identification of goods and services indicates that Applicant's distributorship of "office products" may include computer software, and that all parties offer their goods and services in the same trade channels. Furthermore, the Examining Attorney alleges that Internet evidence attached in both the August 18, 2015 Office Action and the December 9, 2013 Office Action establish that "many entities provide a variety of business goods/services similar to the applicant's and the registrants' services/goods, all in the same trade channels." It was also alleged in the December 9 Office Action that "many entities provide both business services and related educational services, all to the same consumers in the same trade channels." The Examining Attorney has relied on these results to establish confusing similarity between Applicant's business management and distributorship services and the business consulting services and software related goods of LINKAGE and ASIAINFO LINKAGE (Reg. Nos. 2,463,209, 4,425,909, and 4,425,910).

Business Consulting and Business Management

In regard to the consulting and management services, it should first be noted that the Examining Attorney's evidence from the December 9 and August 18 Office Actions produced six examples of entities that only offer consulting services, one example of an entity that only offers management services, and six examples of entities that offer both consulting and management services. Applicant has supplemented that evidence with three additional examples of entities that only offer consulting services in connection with senior care living facilities, and another entity that only offers general business consulting services. Furthermore, the registrants of LINKAGE and ASIAINFO LINKAGE only offer consulting services. In light of this

combined evidence, it cannot be said that business consulting and business management are so related that consumers will generally expect that they are provided by the same source. In fact, the Examining Attorney's allegation that education services are also related to the foregoing provides key insight into the difference between consulting and management services.

Consulting is defined as "employed or involved in giving professional advice to the public or to those practicing the profession." Exhibit XX. Accordingly, consultants are comparable to educators, which is why many consultants may also offer seminars or other educational programming. Thus, it is arguable that consulting and educational services are related.

Management is defined as "the act or manner of managing; handling, direction or control... the person or persons controlling and directing the affairs of a business, institution..." See Dictionary Definitions of Consulting attached hereto as **Exhibits P-Q**. Accordingly, managers are not comparable to either consultants or educators. Notwithstanding, some consultants may also have knowledge or expertise in management or any other "profession," just as some educators may have knowledge or expertise in numerous professions. However, the typical consumer would not expect that every consultant or educator would also offer to manage the consumer's business, laboratory, engineering department, political campaign, etc. Indeed, neither of the owners of the registered marks expects that, which is why they do not offer management services. Instead, LINKAGE is offered in connection with consultation on various business, employment and leadership development services, and ASIAINFO LINKAGE is offered in connection with consultation on various internet technology, computer software/networking, and communications services.

The distinction between consulting services and management services is further evidenced by the TMEP's January 1, 2002 revision (*see* TMEP §1402.11(e)), which explains that consulting services can apply to any type of good or service, not just business management. The merit of this distinction is further demonstrated by the concurrent registrations of the marks INTEGRITY (Reg. 3,134,629) and INTEGRITY CONSULTING (Reg. No. 4,079,901, consulting disclaimed), both in International Class 36, and both relating to the insurance industry. However, INTEGRITY CONSULTING is registered in connection with consultants who assist others with adjusting insurance claims, while INTEGRITY is registered in connection with the actual insurance underwriting service provided by the insurance company. Similarly, ORION and design (Reg. No. 2,635,341) is registered in connection with business management services in the field of information technology systems, but a concurrent registration of ORION and design (Reg. No. 4,267,316) was allowed in connection with business consultation services.

In light of the foregoing, there is no inherent relationship between business consulting and business management such that consumers would expect that a single source (e.g. a consulting firm) would provide both, just as there is no inherent relationship between business education and business management such that consumers would expect that a single source (e.g. a college of management) would provide both.

Office Products and Computer Software

In regard to office products and computer software, Applicant submits that the Examining Attorney's contention that "office products" may include computer software is incorrect. According to TMEP §1402.03(d), identifications of goods for computer programs must be "specific." Applicant's broad identification of "office products" would not satisfy the TMEP's specificity requirement for computer programs, and thus could not be held to include

computer programs. Instead, Applicant's inclusion of "office products" would refer to other generic products, such as pens, paper, notepads, folders, and various other such products found in a typical office that do not carry a similar specificity requirement.

Even if the TMEP did not have the specificity requirement, under the analysis in *Electronic Data Systems Corporation*, 23 U.S.P.Q.2D at 1463, the mere fact that Applicant's services might involve distribution of computer software would not be enough to establish that consumers would believe that such software and the software offered under ASIAINFO LINKAGE emanated from the same source. Applicant's distribution of office products is only "for senior living organizations that serve the aging population both on and off of their senior living campuses," whereas the registrant's software is undeniably being used in connection with e-commerce, customer relations, global computer networking, data analysis, and communications. Given the prevalent belief throughout popular culture that senior citizens are not "tech savvy," it is inconceivable that computer software for senior citizen retirement communities could possibly be confused with highly sophisticated global commerce, network and communications software.

In light of the foregoing, there is no inherent relationship between the highly specific and sophisticated computer software of registrant and Applicant's distributorship of office products to senior citizen retirement communities such that consumers would believe that they emanated from a single source.

B) Registrant's Dietary/Nutritional Supplement/Component Goods and Applicant's Distributorship Services Are Not Related.

The Examining Attorney has alleged that the broad identification of goods and services indicates that Applicant's distributorship of "food, medical supplies, and pharmacy products" may include supplements, and that all parties offer their goods and services through the same

trade channels. As before, the Examining Attorney alleged that attached internet evidence establishes that “many entities provide both supplements and related services,” including retail/distributorship services. The Examining Attorney has relied on these results to establish confusing similarity between Applicant’s distributorship services and the production or manufacturing of supplements by A-LINKAGE (Reg. No. 3,379,376).

The Examining Attorney’s analysis errs because its allegation speaks to a “possibility of confusion” rather than a “likelihood of confusion,” as explained in *Electronic Design & Sales, Inc. v. Electronic Data Systems Corp.*, 954 F.2d 713, 716-719 (Fed. Cir. 1992). In that case, which also dealt with a comparison of arguably related goods and services, the Federal Circuit held that it is erroneous to deny registration merely because “applicant sells some of its goods in some of the same fields in which opposer provides its services.” *Id.* at 716. Here, the Examining Attorney has denied registration because Applicant allegedly sells some of its services in some of the same fields in which registrant provides its goods. Instead, the Examining Attorney must consider the identity of the “relevant persons” who are likely or unlikely to be confused. *Id.*

As an initial matter, it should be acknowledged that registrant’s identification of goods and services is drafted in such a way that multiple interpretations are possible in regard to the goods being offered under International Class 5. A comprehensive reading of all goods and all classes within the registrant’s identification strongly indicates that it has sought to register “component” supplements, and not consumer end-products. This indication is, in fact, confirmed via perusal of the registrant’s websites and other materials, which unambiguously state that it sells component supplements to manufacturers of consumer products. Exhibit XX. Thus, there is no question as to the fact that registrant’s “relative persons” are buyers at consumer product

manufacturing companies. In that context, there is no overlap with Applicant's relative persons, who are buyers of pharmaceutical products or medical supplies at retirement home communities.

This discrepancy may be solved for the purposes of this office action reply by an acknowledgement that the technical definition of "supplement" does not, in fact, include pharmaceutical products or medical supplies. Instead, supplement is defined as "something added to complete a thing, supply a deficiency, or reinforce or extend a whole." See Dictionary Definitions of Supplement attached hereto as **Exhibits R-S**. In that context, it is clear that the registrant's good is a "component" that is added to complete products, i.e., vitamins, fruit drinks and fruit juices and syrups, and oils and cosmetics.

Notwithstanding the foregoing, which is not in dispute based upon the attached evidence, even if it were assumed that the registrant were in the business of producing finished consumer products, under the *Electronic Design & Sales, Inc.* decision, it would not be sufficient to simply show some potential overlap between production and distribution of the goods – the Examining Attorney would still be required to show that the "relevant person" was the same and would be likely to believe that the finished product and distributorship services emanated from a single source. Such a person would have to be a buyer at a retirement home community who is sophisticated enough to purchase pharmaceutical goods directly from the manufacturer but unsophisticated enough to confuse that manufacturer with a distributor of general goods ranging from office products to paint. This seems highly unlikely.

C) Registrant's Agricultural, Fruit and Vegetable Goods and Applicant's Distributorship Services Are Not Related.

As before, the Examining Attorney alleged that attached internet evidence establishes that "many entities provide their own private label brands of foods and similar foods of others in the same trade channels." The Examining Attorney relied on these results to establish confusing

similarity between Applicant's distributorship services and the production of agricultural, fruit and vegetable goods by LINKAGE (Reg. No. 4,533,656).

Again, the Examining Attorney's analysis errs because its allegation speaks to a "possibility of confusion" rather than a "likelihood of confusion." *Electronic Design & Sales, Inc.*, 954 F.2d at 716-719. The Examining Attorney has denied registration because Applicant allegedly sells some of its services in some of the same fields in which registrant provides its goods, but the Examining Attorney must consider the identity of the "relevant persons" who are likely or unlikely to be confused. *Id.*

As noted above, the relevant person for purposes of Applicant's distributorship services would be a buyer at a senior retirement home community who is purchasing a wide range of general products from a distributor. Even if one were to assume that the foods being purchased through Applicant's distributor services and the foods sold by a producer of agricultural, fruits and vegetable products were the same in some instances, it seems similarly highly unlikely that the buyer would have enough knowledge to find and purchase such food directly from a producer but be ignorant enough to believe that the same producer was also distributing office products and paint. Were Applicant only distributing food, the analysis would be closer, but as the Federal Circuit stated in *Electronic Design & Sales, Inc.* "[w]e are not concerned with mere theoretical possibilities of confusion, deception, or mistake or with de minimis situations but with the practicalities of the commercial world, with which the trademark laws deal." 954 F.2d at 717.

IV. The Customer Bases and Channels of Trade Are Inherently Distinct Such That Confusion is Not Likely to Occur.

Because the goods and services at issue are so inherently distinct, the channels of trade and ultimate customer for these services are also inherently distinct and do not overlap *at all*.

Where the channels of trade and ultimate customer for the services are dissimilar, this significantly lessens the possibility of any confusion. See *Frehling Enters., inc. v. Int'l Select Gp., Inc.*, 52 USPQ2d 1447 (11th Cir. 1999); *M2 Software, Inc. v. Madacy Entertainment*, 76 USPQ2d 1161 (9th Cir. 2005) (finding no triable issue of likelihood of confusion and finding the channels of trade factor to weigh "strongly" in defendant's favor where only one party sold its products in retail outlets).

As set forth at length above, Applicant is offering distinct services through distinct channels of trade and to entirely separate consumers. Applicant's consumers can readily discern between distributorship services for senior living communities with dietary supplements, computer software for billing and management, business and performance management consulting and education, and agricultural seeds. Therefore, the cited registrations and Applicant do not offer their goods and services in the same channels of trade and confusion is not likely to occur. See *Oxford Industries, inc. v. JBJ Fabrics, Inc.*, 6 USPQ2d 1756 (SDNY 1988) (no confusion likely where plaintiff sold garments through retail channels to consumers and defendant, a fabric printer, sold fabric to garment manufactures).

V. Applicant's Consumers and Those of the Cited Registrations are Highly Sophisticated.

When comparing the marks at issue, "if the goods or services in question are not related or marketed in such a way that they would be encountered by the same persons in situations that would create the incorrect assumption that they originate from the same source, then, even if the marks are identical, confusion is not likely." See e.g. *Coach Servs., Inc. v. Triumph Learning LLC*, 101 U.S.P.Q.2d 1713, 1723 (Fed. Cir. 2012); *Shen Mfg. Co. v. Ritz Hotel Ltd.*, 73 U.S.P.Q.2d 1350, 1356 (Fed. Cir. 2004); *Local Trademarks, Inc. v. Handy Boys Inc.*, 16 U.S.P.Q.2d 1156, 1158 (T.T.A.B. 1990); *Quartz Radiation Corp. v. Comm/Scope Co.*, 1

U.S.P.Q.2d 1668, 1669 (T.T.A.B. 1986). Further, where “parties sell their goods [or services] to discriminating purchasers under conditions calculated to ensure care in discerning the source or origin of the goods,” confusion is not likely. *Industrial Nucleonic's Corp. v. Hinde*, 177 U.S.P.Q. 386, 387 (C.C.P.A. 1973).

Here, confusion is even less likely to arise because, in each instance, the goods and services at issue are offered to highly discerning consumers through distinct channels of trade. A simple review of the identifications for each mark reveals the inherent sophistication of the consumers being offered. Specifically, Applicant is offering distributorship of a range of products and business management services tailored specifically to senior living communities. These are sophisticated services not utilized by the standard consumer but professionals in the elder care industry, who are by their very nature more discerning than your standard consumer.

This is equally true for each registrant, as follows:

The owner of LINKAGE (Reg. No. 2,463,209) is engaged in business consulting services, with an emphasis on employer/employee relations, leadership/career development, human resources, and education in connection therewith. The buyers of these services are highly sophisticated business owners and professionals.

The owner of ASIAINFO LINKAGE and design (Reg. Nos. 4,425,909 and 4,425,910) is engaged in the production of computer software for e-commerce, customer relations, global networking and communications, and various types of data analytics, among other things. Likewise, the owner of these marks offers business intelligence consulting services. Buyers of these goods and services are also highly sophisticated business owners and professionals, as well as technology experts.

The owner of A-LINKAGE (Reg. No. 3,379,376) is engaged in the production of high-grade supplement components, minerals, and other materials which are used for pharmaceutical products. Buyers of these goods are among the most sophisticated.

The owner of LINKAGE (Reg. No. 4,533,656) claims to produce various types of unprocessed and raw agricultural goods. It is clear from the description that these goods are not being produced for the general consumer, but for a specialized consumer who requires seeds and raw or fresh agricultural products, possibly farmers or those otherwise engaged in agriculture or horticulture. It is most likely that the purchasers of these goods are fairly sophisticated.

Accordingly, the goods and services are all offered to highly discerning consumers who are less likely to be confused overall. Confusion between Applicant's mark and the cited registrations is therefore, not likely to arise.

VI. The High Level of Coexistence for the Term "Linkage" Indicates Weak Protection

Third-party registrations may be relevant to show that a mark or a portion of a mark is descriptive, suggestive, or so commonly used that the public will look to other elements to distinguish the source of the goods or services. See, e.g., *In re Hartz Hotel Servs., Inc.*, 102 USPQ2d 1150, 1153-54 (TTAB 2012); *In re Melville Corp.*, 18 USPQ2d 1386, 1388 (TTAB 1991); *In re Dayco Products-Eagle Motive Inc.*, 9 USPQ2d 1910, 1911-12 (TTAB 1988); *Plus Prods. v. Star-Kist Foods, Inc.*, 220 USPQ 541, 544 (TTAB 1983).

As noted in the previous Office Action response, there is extensive coexistence of marks featuring "LINKAGE" alone or in connection with other marks found active on the Principal Register. While Applicant is mindful that prior determinations are not binding on the Office, nonetheless, given the strong public policy in favor of consistency of decisions, the coexistence of those previously identified marks and the cited registrations is highly persuasive evidence that Applicant's mark can also coexist. Indeed, during the course of this prosecution, the Examining

Attorney has cited at least 10 different coexisting registrations incorporating the word “LINKAGE,” many of which exist in the same classes and provide goods and services that are arguably related. Given Applicant’s highly distinguishable and unique design and wording elements, narrowly tailored services, and specific channels of trade focusing on senior living communities, Applicant’s mark should also be able to coexist

VII. Conclusion.

In light of the arguments set forth above, Applicant respectfully submits that its LINK·AGE CONNECTING RESOURCES FOR THE AGING & Design mark present no likelihood of confusion with the cited registrations. Therefore, Applicant requests that the Examining Attorney consider this Request for Reconsideration, withdraw the Final Refusal, and pass Applicant’s mark to publication.



definitions linkage



Star icon, CITE, A>あ, f, Twitter, g+

linkage

[ling-kij]

Spell Syllables

Examples Word Origin

noun

1. the act of linking; state or manner of being linked.
2. a system of links.
3. *Genetics.* an association between two or more genes on a chromosome that tends to cause the characteristics determined by these genes to be inherited as an inseparable unit.
4. *Machinery.* an assembly of four or more rods for transmitting motion, usually in the same plane or in parallel planes.
5. a factor or relationship that connects or ties one thing to another; *link* : *Administration officials sought to establish linkage between grain sales and relaxed immigration laws.*
6. any of various mathematical or drawing devices consisting of a combination of bars or pieces pivoted together so as to turn about one another, usually in parallel planes.

Word of the Day

castellated

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Difficulty index for linkage



Some English speakers likely know this word

Word Value for linkage



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Why do some people use 'deprecated' to ...



Eitable
When 'inevitable' isn't



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chico's

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ZENERGY®



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linkage

noun | link-age | \ˈlɪŋ-kij\

Simple Definition of LINKAGE

Popularity: Bottom 40% of words

: a connection or relationship between two or more things

Full Definition of LINKAGE

- 1 : the manner or style of being united; as
 - a : the manner in which atoms or radicals are **linked** in a molecule
 - b : **BOND** 3c
- 2 : the quality or state of being linked; *especially* : the relationship between genes on the same chromosome that causes them to be inherited together — compare **MENDEL'S LAW** 2
- 3 : a system of **links**; *especially* : a system of links or bars which are jointed together and more or less constrained by having a link or links fixed and by means of which straight or nearly straight lines or other point paths may be traced
- 4 : **LINK** 2b
- 5 : the tactic in diplomatic negotiations of **linking** often unrelated issues so that progress in one area is dependent on agreement in another

WORD OF THE DAY

FEBRUARY 16, 2016

sub rosa

secretly or in confidence

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BROWSE DICTIONARY

link

linkable

linkage





link

noun | ˈlɪŋk

Definition of LINK

Popularity: Bottom 50% of words

- 1 : a connecting structure: as
 - a (1) : a single ring or division of a chain (2) : one of the standardized divisions of a surveyor's chain that is 7.92 inches (20.1 centimeters) long and serves as a measure of length
 - b : CUFF LINK
 - c : BOND 3C
 - d : an intermediate rod or piece for transmitting force or motion; *especially* : a short connecting rod with a hole or pin at each end
 - e : the fusible member of an electrical fuse
- 2 : something analogous to a link of chain: as
 - a : a segment of sausage in a chain
 - b : a connecting element or factor <found a *link* between smoking and cancer>
 - c : a unit in a communication system
 - d : an identifier attached to an element (as an index term) in a system in order to indicate or permit connection with other similarly identified elements ; *especially* : one (as a hyperlink) in a computer file

WORD OF THE DAY

FEBRUARY 16, 2016

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BROWSE DICTIONARY



definitions link

link¹

[link]

Spell Syllables

Synonyms Examples Word Origin

noun

- one of the rings or separate pieces of which a chain is composed.
- anything serving to connect one part or thing with another; a bond or tie:
The locket was a link with the past.
- a unit in a communications system, as a radio relay station or a television booster station.
- any of a series of sausages in a chain.
- a cuff link.
- a ring, loop, or the like:
a link of hair.
- Computers.* an object, as text or graphics, linked through hypertext to a document, another object, etc.

verb (used with or without object)

- to join by or as if by a link or links; connect; unite (often followed by *up*):
The new bridge will link the island to the mainland. The company will

★

CITE

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g+

Word of the Day

castellated



Difficulty index for link



All English speakers likely know this word

Word Value for link

8

Scrabble

10

Words With

Feedback

Definition of Age by Merriam-Webster

- : the amount of time during which a person or animal has lived
- : the amount of time during which a thing has existed
- : the time of life when a person does something or becomes legally able to do something

Full Definition of age

1. *1 a* : the time of life at which some particular qualification, power, or capacity arises or rests <*the voting age is 18*>; *specifically* : [majority](#) *b* : one of the stages of life *c* : the length of an existence extending from the beginning to any given time <*a boy 10 years of age*> *d* : [lifetime](#) *e* : an advanced stage of life
2. *2* : a period of time dominated by a central figure or prominent feature <*the age of Pericles*>; *as a* : a period in history or human progress <*the age of reptiles*> <*the age of exploration*> *b* : a cultural period marked by the prominence of a particular item <*entering the atomic age*> *c* : a division of geologic time that is usually shorter than an epoch
3. *3 a* : the period contemporary with a person's lifetime or with his or her active life *b* : a long time — usually used in plural <*haven't seen him in ages*> *c* : [generation](#)
4. *4* : an individual's development measured in terms of the years requisite for like development of an average individual

See [age](#) defined for English-language learners

See [age](#) defined for kids

Examples of age

1. Some people are reluctant to reveal their *ages*.
2. She died tragically at a young *age*.
3. The treatment depends on the sex and *age* of the patient.
4. She died at the *ripe old age* of 90.
5. The movie appeals to people *of all ages*.
6. Their son needs to spend more time with children his own *age*.
7. a group of children ranging in *age* from 8 to 11

8. She became involved with a man twice her *age*.
9. The program is for people over *age* 50.
10. groups of people classified by race and *age*

Origin of *age*

Middle English, from Anglo-French *aage*, *age*, from Vulgar Latin **aetaticum*, from Latin *aetat-*, *aetas*, from *aevum* lifetime — more at [ave](#)

First Known Use: 13th century



Word of the Day (<http://dictionary.reference.com/wordoftheday>)

wordoftheday)

Translate (<http://translate.reference.com/>)

Games (<http://dictionary.reference.com/fun>)

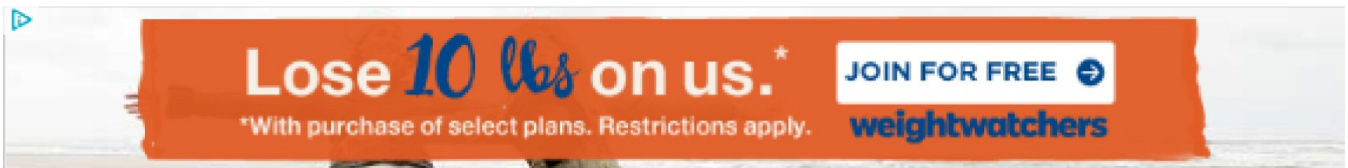
Blog (<http://blog.dictionary.com/>)

(<http://dictionary.reference.com/>)

)

definitions ▾

age



age (<http://static.sfdict.com/staticrep/dictaudio/A02/A0205900.mp3>)

[eyj]

Synonyms Examples Word Origin

noun

<http://dictionary.reference.com/browse/age>

1. the length of time during which a being or thing has existed; length of life or existence to the time spoken of or referred to:
trees of unknown age; His age is 20 years.
2. a period of human life, measured by years from birth, usually marked by a certain stage or degree of mental or physical development and involving legal responsibility and capacity:
the age of discretion; the age of consent; The state raised the drinking age from 18 to 21 years.
3. the particular period of life at which a person becomes naturally or conventionally qualified or disqualified for anything:
He was over age for military duty.

4. one of the periods or stages of human life:
a person of middle age.
 5. advanced years; old age:
His eyes were dim with age.
 6. a particular period of history, as distinguished from others; a historical epoch:
the age of Pericles; the Stone Age; the age of electronic communications.
 7. the period of history contemporary with the span of an individual's life:
He was the most famous architect of the age.
-

verb (used without object), **aged, aging** or **ageing**.

15. to grow old:
He is aging rapidly.
16. to mature, as wine, cheese, or wood:
a heavy port that ages slowly.

verb (used with object), **aged, aging** or **ageing**.

17. to make old; cause to grow or seem old:
Fear aged him overnight.
18. to bring to maturity or a state fit for use:
to age wine.
19. to store (a permanent magnet, a capacitor, or other similar device) so that its electrical or magnetic characteristics become constant.
20. to expose (a dye or dyed cloth) to steam or humid air in order to fix the dye.
21. to stabilize the electrical properties of (a device) by passing current through it.

Idioms

22. **of age**, *Law*.

- a. being any of several ages, usually 21 or 18, at which certain legal rights, as voting or marriage, are acquired.
- b. being old enough for full legal rights and responsibilities.

Origin of age

ish

[onary.reference.com/browse/Middle%20English](http://dictionary.reference.com/browse/Middle%20English))

Old French

(<http://dictionary.reference.com/browse/Old%20French>)

1225-1275

1225-75; (noun) Middle English < Anglo-French, Old French *aage*, *eage*, equivalent to *aé* (< Latin *aetātem* accusative of *ae* (*vi*) *tās* age; *aev* (*um*) time, lifetime + *-itās* -ity (<http://dictionary.reference.com/browse/-ity>)) + *-age* -age (<http://dictionary.reference.com/browse/-age>); (v.) Middle English *agen*, derivative of the noun

Related forms

interage, adjective

preage, verb, preaged, preaging.

subage, noun

unaging, adjective

Synonyms

6. Age, epoch, era, period all refer to an extent of time. Age usually implies a considerable extent of time, especially one associated with a dominant personality, influence, characteristic, or institution: *the age of chivalry*. Epoch and era are often used interchangeably to refer to an extent of time characterized by changed conditions and new undertakings: *an era(or epoch) of invention*. epoch sometimes refers especially to the beginning of an era: *the steam engine—an*

-age

1. a suffix typically forming mass or abstract nouns from various parts of speech, occurring originally in loanwords from French (*voyage; courage*) and productive in English with the meanings "aggregate" (*coinage; peerage; trackage*), "process" (*coverage; breakage*), "the outcome of" as either "the fact of" or "the physical effect or remains of" (*seepage; wreckage; spoilage*), "place of living or business" (*parsonage; brokerage*), "social standing or relationship" (*bondage; marriage; patronage*), and "quantity, measure, or charge" (*footage; shortage; tonnage; towage*).

Origin

Middle English < Old French < Latin *-āticum*, neuter of *-āticus* adj. suffix; an extension of Latin *-āta* -ate (<http://dictionary.reference.com/browse/-ate>)¹, whose range of senses it reflects closely

Ag.E.

1. Agricultural Engineer.

A.G.E.

1. Associate in General Education.

Dictionary.com Unabridged

Based on the Random House Dictionary, © Random House, Inc. 2016.

Cite This Source (<http://dictionary.reference.com/cite.html?qh=age&ia=luna>)

Examples from the Web for age

Contemporary Examples

Inflating his *age* by a year (in reality turning 20 at the time), Moon was determined make his birthday a smash.

(<http://www.thedailybeast.com/speed-read-11-most-shocking-moments-from-pete-townshend-s-who-i-am>)
(<http://www.thedailybeast.com/articles/2012/10/08/speed-read-11-most-shocking-moments-from-pete-townshend-s-who-i-am.html?source=dictionary>)

Abby Haglage (<http://www.thedailybeast.com/contributors/abby-haglage.html?source=dictionary>)

October 7, 2012

The timing that served Pastras so well that he swam in the 2004 Athens Olympics at the *age* of just 18 has deserted him.

(<http://www.thedailybeast.com/greece-s-youth-in-crisis>)
(<http://www.thedailybeast.com/articles/2011/11/22/greece-s-youth-in-crisis.html?source=dictionary>)

(<http://www.thedailybeast.com/contributors/.html?source=dictionary>)

November 21, 2011

In an *age* that was all about "sell, sell, sell," it is no wonder that it had become increasingly acceptable to sell oneself.

British Dictionary definitions for age

age

/eɪdʒ/

noun

1. the period of time that a person, animal, or plant has lived or is expected to live: *the age of a tree, what age was he when he died?, the age of a horse is up to thirty years*
2. the period of existence of an object, material, group, etc: *the age of this table is 200 years*
3. a. a period or state of human life: *he should know better at his age, she had got beyond the giggly age*
b (as modifier): *age group*

-age

suffix

1. indicating a collection, set, or group: *acreage, baggage*
2. indicating a process or action or the result of an action: *haulage, passage, breakage*

Collins English Dictionary - Complete & Unabridged 2012 Digital Edition

© William Collins Sons & Co. Ltd. 1979, 1986 © HarperCollins

Publishers 1998, 2000, 2003, 2005, 2006, 2007, 2009, 2012

Cite This Source (<http://dictionary.reference.com/cite.html?qh=age&ia=cad2>)

Word Origin and History for age

n.

late 13c., "long but indefinite period in human history," from Old French *aage* (11c., Modern French *âge*) "age; life, lifetime, lifespan; maturity," earlier *edage*, from Vulgar Latin **aetaticum* (source of Spanish *edad*, Italian *età*, Portuguese *idade* "age"), from Latin *aetatem* (nominative *aetas*), "period of life, age, lifetime, years," from *aevum* "lifetime, eternity, age," from PIE root **aiw-* "vital force, life, long life, eternity" (see *eon* (/browse/eon)). Meaning "time something has lived, particular length or stage of life" is from early 14c. Used especially for "old age" since early 14c. Expelled native *eld*.

v.

"to grow old," late 14c., from *age* (/browse/age) (*n.*). Meaning "to make old" is early 15c. Related: Aged (/browse/Aged); *aging*.

-age

word-forming element in nouns of act, process, function, condition, from Old French and French *-age*, from Late Latin *-aticum* "belonging to, related to," originally neuter adjectival suffix, from Latin *-atus*, pp. suffix of verbs of the first conjugation.

Online Etymology Dictionary, © 2010 Douglas Harper

Cite This Source (<http://dictionary.reference.com/cite.html?qh=age&ia=etymon2>)

age in Medicine

age (āj)

n.

The length of time that one has existed; duration of life. *v.*

1. To become old.
2. To manifest traits associated with old age.

The American Heritage® Stedman's Medical Dictionary

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Related Abbreviations for age

AGE

acute gastroenteritis

Ag.E.

1. agricultural engineer
2. agricultural engineering

The American Heritage® Abbreviations Dictionary, Third Edition

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Cite This Source (<http://dictionary.reference.com/cite.html?qh=age&ia=ahabb2>)

age in the Bible

used to denote the period of a man's life (Gen. 47:28), the maturity of life (John 9:21), the latter end of life (Job 11:17), a generation of the human race (Job 8:8), and an indefinite period (Eph. 2:7; 3:5, 21; Col. 1:26). Respect to be shown to the aged (Lev. 19:32). It is a blessing to communities when they have old men among them (Isa. 65:20; Zech. 8:4). The aged supposed to excel in understanding (Job 12:20; 15:10; 32:4, 9; 1 Kings 12:6, 8). A full age the reward of piety (Job 5:26; Gen. 15:15).

Easton's 1897 Bible Dictionary

Cite This Source (<http://dictionary.reference.com/cite.html?qh=age&ia=easton>)

Idioms and Phrases with age

age

see:

act one's age (/browse/act one's age)

coon's age (/browse/coon's age)

golden age (/browse/golden age)

in this day and age (/browse/in this day and age)

of age (/browse/of age)

ripe old age (/browse/ripe old age)

under age (/browse/under age)

The American Heritage® Idioms Dictionary

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Int. Cl.: 9

Prior U.S. Cls.: 21, 23, 26, 36, and 38

Reg. No. 2,987,704

United States Patent and Trademark Office

Registered Aug. 23, 2005

**TRADEMARK
PRINCIPAL REGISTER**

ASIAINFO

ASIAINFO HOLDINGS, INC. (DELAWARE CORPORATION)

5201 GREAT AMERICAN PARKWAY

SUITE 429

SANTA CLARA, CA 95054

FOR: COMPUTER SOFTWARE, NAMELY SOFTWARE DESIGNED FOR ACCOUNTING AND CUSTOMER RELATIONSHIP MANAGEMENT IN THE FIELD OF TELECOMMUNICATIONS; AND SOFTWARE DEVELOPMENT TOOLS IN THE FIELD OF

NETWORK MANAGEMENT AND SECURITY, IN CLASS 9 (U.S. CLS. 21, 23, 26, 36 AND 38).

FIRST USE 1-0-2000; IN COMMERCE 1-0-2000.

OWNER OF U.S. REG. NOS. 2,310,503, 2,335,983, AND 2,343,439.

SN 76-287,449, FILED 7-19-2001.

DAHLIA GEORGE, EXAMINING ATTORNEY

Int. Cl.: 9

Prior U.S. Cls.: 21, 23, 26, 36, and 38

United States Patent and Trademark Office

Reg. No. 2,989,918

Registered Aug. 30, 2005

TRADEMARK
PRINCIPAL REGISTER

The logo for AsiaINFO features the word "Asia" in a serif font, followed by "INFO" in a bold, sans-serif font. A stylized graphic element consisting of two slanted parallel lines is positioned above the "I" in "INFO".

ASIAINFO HOLDINGS, INC. (DELAWARE CORPORATION)
5201 GREAT AMERICAN PARKWAY, SUITE 429
SANTA CLARA, CA 95054

FIRST USE 1-0-2000; IN COMMERCE 1-0-2000.

OWNER OF U.S. REG. NOS. 2,310,503, 2,335,983,
AND 2,343,439.

FOR: COMPUTER SOFTWARE, NAMELY SOFTWARE DESIGNED FOR ACCOUNTING AND CUSTOMER RELATIONSHIP MANAGEMENT IN THE FIELD OF TELECOMMUNICATIONS; AND SOFTWARE DEVELOPMENT TOOLS IN THE FIELD OF NETWORK MANAGEMENT AND SECURITY, IN CLASS 9 (U.S. CLS. 21, 23, 26, 36 AND 38).

SN 76-287,554, FILED 7-19-2001.

DAHLIA GEORGE, EXAMINING ATTORNEY

Int. Cl.: 42

Prior U.S. Cls.: 100 and 101

Reg. No. 2,343,439

United States Patent and Trademark Office

Registered Apr. 18, 2000

**SERVICE MARK
PRINCIPAL REGISTER**



ASIAINFO HOLDINGS, INC. (DELAWARE
CORPORATION)
5201 GREAT AMERICAN PARKWAY
SUITE 429
SANTA CLARA, CA 95054

FIRST USE 2-0-1998; IN COMMERCE
2-0-1998.

THE ENGLISH transliteration of the
Chinese characters in the mark is
"ASHIN". The English translation of
the Chinese characters in the mark
is "ASIAINFO".

FOR: COMPUTER CONSULTATION AND IN-
TEGRATION OF COMPUTER SYSTEMS AND
NETWORKS, IN CLASS 42 (U.S. CLS. 100 AND
101).

SER. NO. 75-712,523, FILED 5-24-1999.

PAULA MAHONEY, EXAMINING ATTORNEY

Int. Cl.: 42

Prior U.S. Cls.: 100 and 101

Reg. No. 2,335,983

United States Patent and Trademark Office

Registered Mar. 28, 2000

**SERVICE MARK
PRINCIPAL REGISTER**



ASIAINFO

ASIAINFO HOLDINGS, INC. (DELAWARE
CORPORATION)
5201 GREAT AMERICAN PARKWAY
SUITE 429
SANTA CLARA, CA 95054

NETWORKS, IN CLASS 42 (U.S. CLS. 100 AND
101).

FIRST USE 2-0-1998; IN COMMERCE
2-0-1998.

SER. NO. 75-712,522, FILED 5-24-1999.

FOR: COMPUTER CONSULTATION AND IN-
TEGRATION OF COMPUTER SYSTEMS AND

PAULA MAHONEY, EXAMINING ATTORNEY

Int. Cl.: 42

Prior U.S. Cls.: 100 and 101

Reg. No. 2,310,503

United States Patent and Trademark Office

Registered Jan. 25, 2000

**SERVICE MARK
PRINCIPAL REGISTER**

ASIAINFO

ASIAINFO HOLDINGS, INC. (TEXAS CORPORATION)
5201 GREAT AMERICAN PARKWAY, SUITE
226
SANTA CLARA, CA 95054

NETWORKS, IN CLASS 42 (U.S. CLS. 100 AND 101).

FIRST USE 0-0-1993; IN COMMERCE 0-0-1993.

SER. NO. 75-444,589, FILED 3-4-1998.

FOR: COMPUTER CONSULTATION AND INTEGRATION OF COMPUTER SYSTEMS AND

KARLA PERKINS, EXAMINING ATTORNEY

Int. Cl.: 42

Prior U.S. Cls.: 100 and 101

Reg. No. 2,310,503

United States Patent and Trademark Office

Registered Jan. 25, 2000

**SERVICE MARK
PRINCIPAL REGISTER**

ASIAINFO

ASIAINFO HOLDINGS, INC. (TEXAS CORPORATION)
5201 GREAT AMERICAN PARKWAY, SUITE
226
SANTA CLARA, CA 95054

NETWORKS, IN CLASS 42 (U.S. CLS. 100 AND
101).

FIRST USE 0-0-1993; IN COMMERCE
0-0-1993.

SER. NO. 75-444,589, FILED 3-4-1998.

FOR: COMPUTER CONSULTATION AND IN-
TEGRATION OF COMPUTER SYSTEMS AND

KARLA PERKINS, EXAMINING ATTORNEY



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A-type proanthocyanidin

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A type proanthocyanidins are a specific type of proanthocyanidins, which are a class of flavanoid. Proanthocyanidins fall under a wide range of names in the nutritional and scientific vernacular, including oligomeric proanthocyanidins, flavanoids, polyphenols, condensed tannins, and OPCs. Proanthocyanidins were first popularized by French scientist Jacques Masquelier.^[1]

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Distribution in plants [edit]

A-type linkage is a less common feature in proanthocyanidins with both 4β→8 (B-type) and 2β→O→7 interflavanoid bonds.^[2]

A-type proanthocyanidin glycosides can be isolated from cocoa liquor.^[3]

Dimers [edit]

- Procyanidin A1 is an epicatechin-(2β→O→7, 4β→8)-epicatechin dimer.
- Procyanidin A2 is a dimeric (-)epicatechin.

Other A-type proanthocyanidins can be found in cranberries,^[2] in apricots, in cinnamon,^[4] in *Prunus armeniaca* (ent-epiafzelechin-3-O-p-hydroxybenzoate-(4α→8,2α→O→7)-epiafzelechin) and in peanut skins (epicatechin-(2β→O→7, 4β→8)-ent-epicatechin).^[5]

Epi-afzelechin-(4β→8, 2β→O→7)-afzelechin (geranin A) and epi-catechin-(4β→8, 2β→O→7)-afzelechin (geranin B) can be found in *Geranium niveum*.^[6]

Trimers [edit]

- Selliaguein A is a natural sweetener
- Selliaguein B** can also be isolated from the rhizomes of *Selligaea feei*.^[7]

An A type proanthocyanidins trimer can be found in *Lindera aggregata* (epicatechin-(4β→8,2β→O→7)-entcatechin-(4β-8)-catechin).^[8] This compound shows cytoprotective action against ethanol-induced gastric injury.^[9]

In *Ecdysanthera utilis* (epicatechin-(4β→8,2β→O→7)-epicatechin-(4β→8)-epicatechin and epicatechin-(4β→8)-epicatechin-(4β→8,2β→O→7)-epicatechin-(4β→8)-epicatechin) can be found.^[10]

Chemistry [edit]

B-type procyanidins (catechin dimers) can be converted to A-type procyanidins by radical oxidation.^[11] Fragmentation patterns for A-type proanthocyanidins include **heterocyclic ring fission** (HRF), **retro-Diels-Alder** (RDA) fission, **benzofuran-forming fission** (BFF) and **quinone methide fission** (QM).^[12]

No effect on urinary tract infection [edit]

The metabolism of type-A proanthocyanidins is significant since a large number of metabolites are detected in urine and feces soon after ingestion of foods rich in polymers, indicating rapid elimination and absence of physiological effect. Polymeric type-A proanthocyanidins are depolymerized into epicatechin units in the small intestine, then cleaved into smaller phenolic acids with no known biological role.^[13]

In vitro, A-type proanthocyanidins isolated from cranberry juice cocktail demonstrated anti-adhesion activity against *E. coli* binding to urinary tract epithelial cells, whereas B-type proanthocyanidins from grape exhibited minor activity.^[14] However, in humans, there is no sufficient clinical evidence that cranberry type-A proanthocyanidins are effective in lowering risk of urinary tract infection.^{[15][16]}

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V · T · E	Types of procyanidins	[hide]
A-type proanthocyanidins	Dimers: Procyanidin A1 · A2 · Trimers: Cinnamtannin B1 · Tetramers: Arecatannin A2	
B type proanthocyanidins	Dimers: Procyanidin B1 · B2 · B3 · B4 · B5 · B6 · B8 Trimers: Arecatannin B1 (epicatechin-(4β→8)-epicatechin-(4β→6)-catechin) · Procyanidin C1 (epicatechin-(4β→8)-epicatechin-(4β→8)-epicatechin) · Procyanidin C2 (catechin-(4α→8)-catechin-(4α→8)-catechin)	
Types	Arecatannins (Arecatannin A1 · Arecatannin A3 · Arecatannin B2 · Arecatannin C1)	

Categories: Condensed tannins

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Abstract

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Phytochemistry. 2005 Sep;66(18):2281-91.

A-type cranberry proanthocyanidins and uropathogenic bacterial anti-adhesion activity.

Howell AB¹, Reed JD, Krueger CG, Winterbottom R, Cunningham DG, Leahy M.

Author information

Abstract

Clinical, epidemiological and mechanistic studies support the role of cranberry (*Vaccinium macrocarpon* Ait.) in maintaining urinary tract health. Cranberry proanthocyanidins contain A-type linkages and have been associated with preventing adhesion of P-fimbriated uropathogenic *Escherichia coli* to uroepithelial cells. It is not known if the presence of the A-type linkage is a prerequisite for anti-adhesion activity. Other commercial sources of proanthocyanidins with all B-type linkages have not previously been screened for this activity. The goals of this study were to compare the in vitro anti-adhesion activity of A-linked proanthocyanidins from cranberry juice cocktail with the anti-adhesion activities of B-linked proanthocyanidins from commercial grape and apple juices, green tea and dark chocolate, and determine if anti-adhesion activity is detectable in human urine following consumption of single servings of each commercial food product. Structural heterogeneity and presence of the A-type linkage in cranberry proanthocyanidins was confirmed utilizing MALDI-TOF/MS and DI/ESI MS, as was the presence of all B-type linkages in the proanthocyanidins from the other commercial products. The isolated A-type proanthocyanidins from cranberry juice cocktail elicited in vitro anti-adhesion activity at 60 microg/ml, the B-type proanthocyanidins from grape exhibited minor activity at 1200 microg/ml, while other B-type proanthocyanidins were not active. Anti-adhesion activity in human urine was detected following cranberry juice cocktail consumption, but not after consumption of the non-cranberry food products. Results suggest that presence of the A-type linkage in cranberry proanthocyanidins may enhance both in vitro and urinary bacterial anti-adhesion activities and aid in maintaining urinary tract health.

PMID: 16055161 [PubMed - indexed for MEDLINE]



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Cranberries + Urinary Tract Infections



Many people know that cranberries help maintain urinary tract health. Research is now showing just how cranberry juice promotes urinary tract health...and why cranberries are the only food with this benefit.

For many years, people thought drinking cranberry juice was beneficial because the juice was thought to increase the acidity of urine in the bladder and therefore kill the bacteria that cause urinary tract infections. This is not the case.

It turns out that cranberries contain compounds called proanthocyanidins (PACs) that have strong bacterial anti-adhesion properties. PACs interfere with the ability of bacteria to adhere to the cells that line the bladder wall. Instead of sticking to the bladder wall and causing an infection (and the subsequent pain), the bacteria get flushed out in the urine.

While other foods like apple juice, grape juice and green tea contain proanthocyanidins (PACs), cranberries are the only food that contain PACs with A type linkages (as opposed to B type linkages). The unique molecular structure explains why cranberries are the only food associated with urinary tract health.

E. coli bacteria cause 80-90% of urinary tract infections. Proanthocyanidins (PACs) from cranberries affect E. coli cells in three ways. Cranberry PACs (1) change the shape of the E. coli from rods to spheres, (2) alter the cell membranes, and (3) compress tendrils on the outside of the cells, which affects E. coli's ability to attach to cells lining the bladder wall. All of these effects inhibit the bacteria's ability to attach to cells lining the bladder wall.

The anti-adhesion property of cranberry juice and cranberry juice cocktail has been demonstrated in many lab and human studies. (1-3) However, only one study has examined the anti-adhesion property of sweetened dried cranberries. (4) This small pilot study of five human subjects compared the effects of sweetened dried cranberries and unsweetened raisins. Only the subjects who consumed the dried cranberries exhibited anti-adhesion activity. More research is needed to support this finding, but it looks like sweetened dried cranberries may also help promote urinary tract health.

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Facts about Urinary Tract Infections (UTIs)

- Each year UTIs account for nearly 10 million doctor visits in the U.S.
- One in five U.S. women will have at least one UTI in her lifetime.
- UTIs are caused by bacteria entering the bladder.
- 80-90% of all UTIs are caused by a single type of bacteria, E. coli.
- Women are more likely to develop UTIs than men because women have a shorter urethra, which makes it easier for bacteria to reach the bladder.
- People with diabetes are more susceptible to UTIs.
- Men with enlarged prostate glands are more likely to develop UTIs.
- Left untreated, a UTI can move from the bladder to the kidneys, causing a much more serious infection called pyelonephritis.
- Antibiotics are the most common and effective form of treatment for urinary tract infections.

SOURCE: National Kidney Foundation



Article

A-Type Cranberry Proanthocyanidins Inhibit the RANKL-Dependent Differentiation and Function of Human Osteoclasts

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Abstract: This study investigated the effect of A-type cranberry proanthocyanidins (AC-PACs) on osteoclast formation and bone resorption activity. The differentiation of human pre-osteoclastic cells was assessed by tartrate-resistant acid phosphatase (TRAP) staining, while the secretion of interleukin-8 (IL-8) and matrix metalloproteinases (MMPs) was measured by ELISA. Bone resorption activity was investigated by using a human bone plate coupled with an immunoassay that detected the release of collagen helical peptides. AC-PACs up to 100 µg/mL were atoxic for osteoclastic cells. TRAP staining evidenced a dose-dependent inhibition of osteoclastogenesis. More specifically, AC-PACs at 50 µg/mL caused a 95% inhibition of RANKL-dependent osteoclast differentiation. This concentration of AC-PACs also significantly increased the secretion of IL-8 (6-fold) and inhibited the secretion of both MMP-2 and MMP-9. Lastly, AC-PACs (10, 25, 50 and 100 µg/ml) affected bone degradation mediated by mature osteoclasts by significantly decreasing the release of collagen helical peptides. This study suggests that AC-PACs can interfere with osteoclastic cell maturation and physiology as well as prevent bone resorption. These compounds may be considered as therapeutic agents for the prevention and treatment of periodontitis.

Keywords: proanthocyanidin; cranberry; periodontitis; bone resorption; osteoclast

1. Introduction

The cranberry (*Vaccinium macrocarpon*), a native North American fruit, has been widely investigated for its diverse beneficial effects for human health, primarily those related to its anti-adherence activity [1]. Indeed, cranberry proanthocyanidins, which present a unique oligomeric structure with A-linkage that differs them from B-type proanthocyanidins found in other berry fruits, have been intensively investigated. More specifically, cranberry A-type proanthocyanidins (AC-PACs) demonstrated anti-adhesion effect against *Escherichia coli*, whereas B-type proanthocyanidins from other fruits were devoid of anti-adhesion properties [2,3]. Proanthocyanidin-enriched cranberry extracts have also presented a variety of potential benefits for oral health, such as inhibition of biofilm formation and acid production by cariogenic bacteria [4] as well as modulation of the inflammatory response to periodontopathogens [5] and inactivation of bacteria-related proteolytic enzymes [6]. Additionally, our laboratory showed that AC-PACs were able to inhibit matrix metalloproteinase (MMP) production by human macrophages stimulated with *Aggregatibacter actinomycetemcomitans* lipopolysaccharide (LPS), as well as to reduce MMP-1 and -9 catalytic activities [7]. We have also demonstrated that AC-PACs efficiently neutralized *Porphyromonas gingivalis* virulence properties and modulated the inflammatory response of epithelial cells to this periodontopathogen [8].

The resorption of alveolar bone is a typical hallmark of periodontal disease, a multifactorial disorder triggered by the accumulation of specific bacterial species organized in a biofilm and present in subgingival sites. These periodontopathogens, mostly Gram-negative and strictly anaerobic, are able to stimulate a host immune response, which in turn leads to a destructive inflammatory process [9]. The secretion of proinflammatory mediators, including cytokines, chemokines and prostaglandins, allow the propagation of inflammation within gingival tissues and the expansion of the process to the adjacent alveolar bone [10].

Alveolar bone destruction is mediated by the recruitment and differentiation of osteoclasts into their mature phenotype. These cells derive from hematopoietic monocyte/macrophage precursors under the action of receptor activator of nuclear factor kappa-B ligand (RANKL) and macrophage colony-stimulating factor (M-CSF). Once activated, resorptive osteoclasts attach to the bone surface and promote mineral dissolution by acidification of the sub-osteoclastic microenvironment [11]. Subsequently, the demineralized organic matrix of bone is degraded by secreted proteases such as cathepsin K and MMPs [11]. It has been demonstrated that osteoclastogenesis is enhanced during periodontal disease due to the accumulation of inflammatory cytokines, which will either stimulate osteoclast proliferation or promote the differentiation and maturation of progenitor cells [12,13]. Accordingly, the modulation of osteoclast formation and function is pointed as one of the therapeutic targets in the prevention of alveolar bone loss associated with periodontal disease.

Since AC-PACs present a number of biological activities that might be relevant to the control of tissue destruction occurring in periodontal disease, we hypothesized that these natural compounds can also interfere with bone resorption mediated by osteoclasts. Therefore, the aim of the present study was

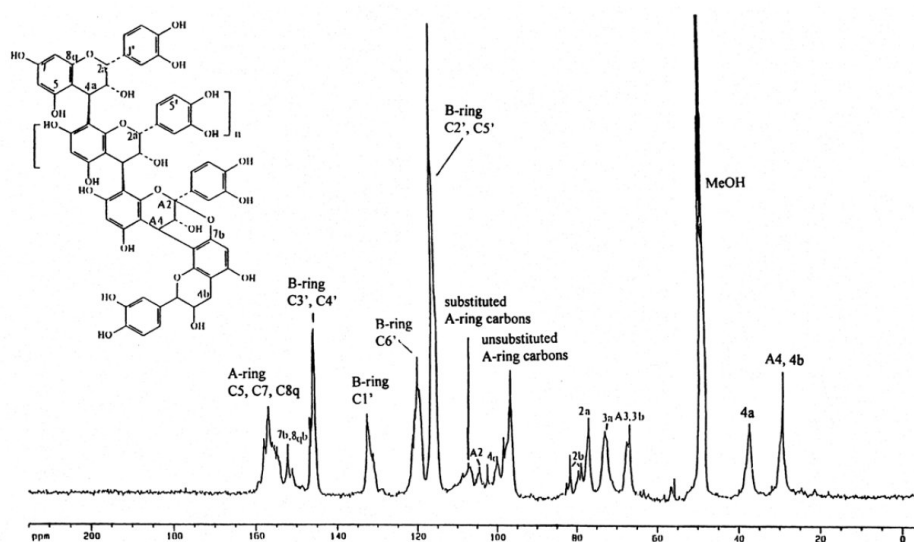
to investigate the effect of AC-PACs on osteoclast differentiation and physiology, as well as on its bone-resorbing activity.

2. Results and Discussion

2.1. A-type cranberry proanthocyanidins

Characterization of the AC-PACs fraction was made by ^{13}C -NMR. As shown in Figure 1, the proanthocyanidin molecules consist of epicatechin units presenting mainly a degree of polymerization (DP) of 4 and 5 and containing at least one A-type linkage, as previously reported [14].

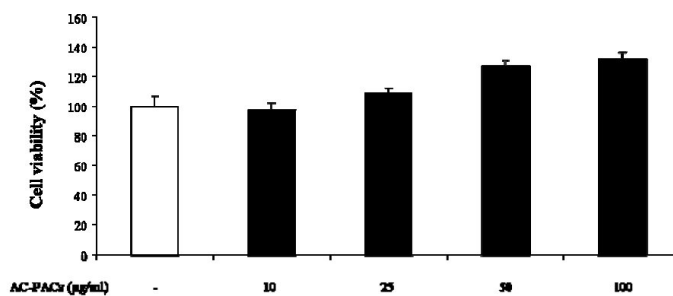
Figure 1. ^{13}C -NMR spectrum of cranberry proanthocyanidins showing the presence of A-type linkages.



2.2. Cytotoxicity

As reported in Figure 2, AC-PACs did not exhibit any detrimental effect on cell viability at concentrations ranging from 10 to 100 $\mu\text{g}/\text{mL}$.

Figure 2. Cytotoxic effect of AC-PACs on osteoclastic cells as measured by the MTT assay.

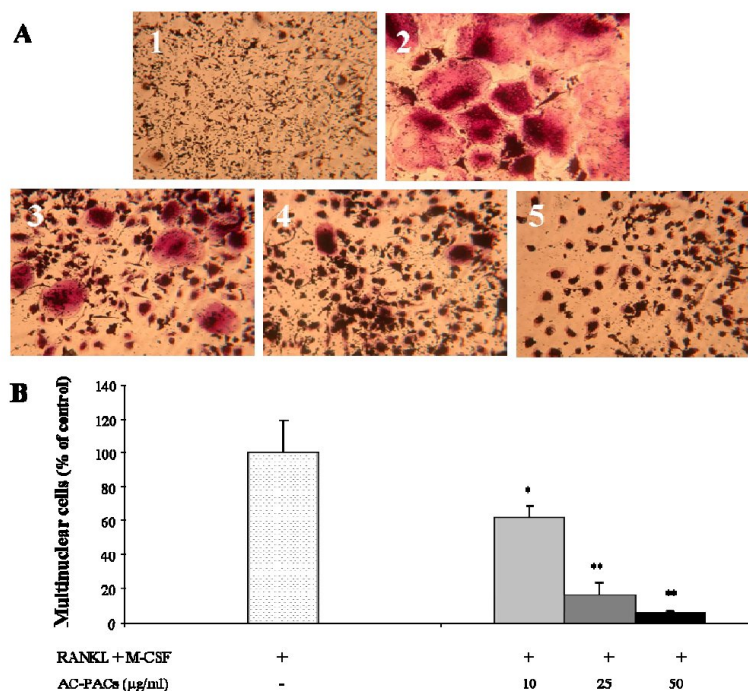


Conversely, a cell proliferation increase of up to $32 \pm 5\%$ was observed at the highest concentrations tested, indicating the absence of any significant toxic effects towards osteoclasts.

2.3. Osteoclast formation

The degree of osteoclast formation was evaluated by quantification of TRAP-positive stained multinucleated cells. Within the range of concentrations tested (10–50 $\mu\text{g/mL}$), AC-PACs were able to decrease the formation of differentiated osteoclasts (TRAP-positive multinucleated cells) in a dose-dependent manner (Figure 3A). A significant inhibition ($p < 0.05$) of osteoclast differentiation could be observed, even when cells were treated with the lowest concentration of AC-PACs (10 $\mu\text{g/mL}$) (Figure 3B). More specifically, AC-PACs at final concentrations of 10, 25 and 50 $\mu\text{g/mL}$ caused an inhibition on cell maturation of $38 \pm 7\%$, $84 \pm 7\%$, and $95 \pm 1\%$, respectively (Figure 3B). The impairment of the maturation process of pre-osteoclastic cells after being exposed to both RANKL and M-CSF suggests that AC-PACs may hamper osteoclast formation.

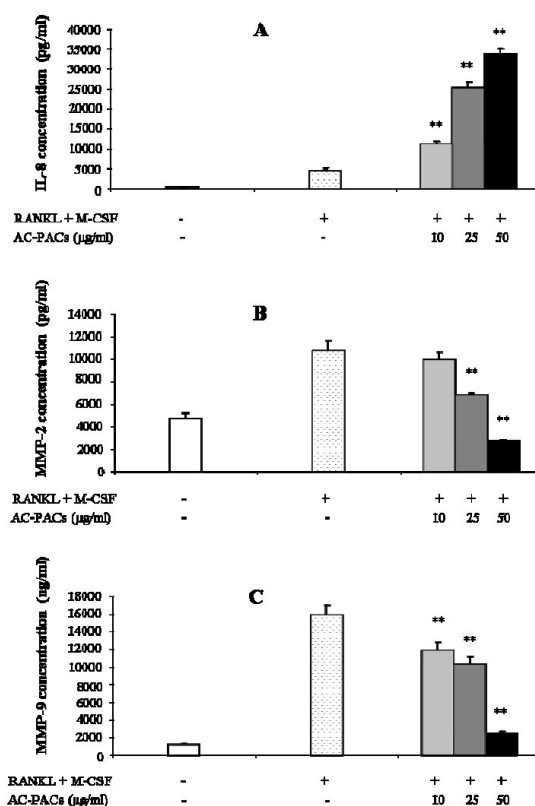
Figure 3. Inhibitory effect of AC-PACs on the differentiation of human pre-osteoclasts. Cells were treated with various concentrations of AC-PACs and cultivated in the presence of both M-CSF and RANKL. **(A)** TRAP staining was performed to evidence multinuclear cells. 1) Cells treated with M-CSF only (negative control); 2) Cells treated with M-CSF + RANKL (positive control); 3) Cells treated with M-CSF + RANKL + 10 $\mu\text{g/mL}$ AC-PACs; 4) Cells treated with M-CSF + RANKL + 25 $\mu\text{g/mL}$ AC-PACs; 5) Cells treated with M-CSF + RANKL + 50 $\mu\text{g/mL}$ AC-PACs. **(B)** % of multinuclear TRAP-stained cells: Control – 100%; 10 $\mu\text{g/mL}$ AC-PAC – $62 \pm 7\%$; 25 $\mu\text{g/mL}$ AC-PAC – $16 \pm 7\%$; 50 $\mu\text{g/mL}$ AC-PAC – $5 \pm 1\%$. * $p < 0.05$, ** $p < 0.01$.



2.4. Interleukin and matrix metalloproteinase secretion

The effect of AC-PACs on the secretion of IL-8, a mediator involved in osteoclastogenesis, and MMP-2 and -9, proteinases related to the resorptive activity of osteoclasts, is reported in Figure 4. IL-8 secretion was significantly increased by AC-PACs at 10, 25 and 50 $\mu\text{g}/\text{mL}$ by 2-, 6- and 7-fold, respectively (Figure 4A). Conversely, treatment of osteoclast cells with AC-PACs at 25 and 50 $\mu\text{g}/\text{mL}$ decreased the levels of MMP-2 production by $36 \pm 2\%$ and $75 \pm 1\%$, respectively (Figure 4B). MMP-9 secretion was also significantly reduced by AC-PACs treatment at 10, 25 and 50 $\mu\text{g}/\text{mL}$ (Figure 4C), showing inhibition levels of 25 ± 6 , 35 ± 5 and $84 \pm 1\%$, respectively.

Figure 4. Effect of AC-PACs on secretion of IL-8 and MMPs by osteoclastic cells treated with AC-PACs. **(A)** IL-8 secretion. **(B)** MMP-2 secretion. **(C)** MMP-9 secretion. ****** $p < 0.01$.



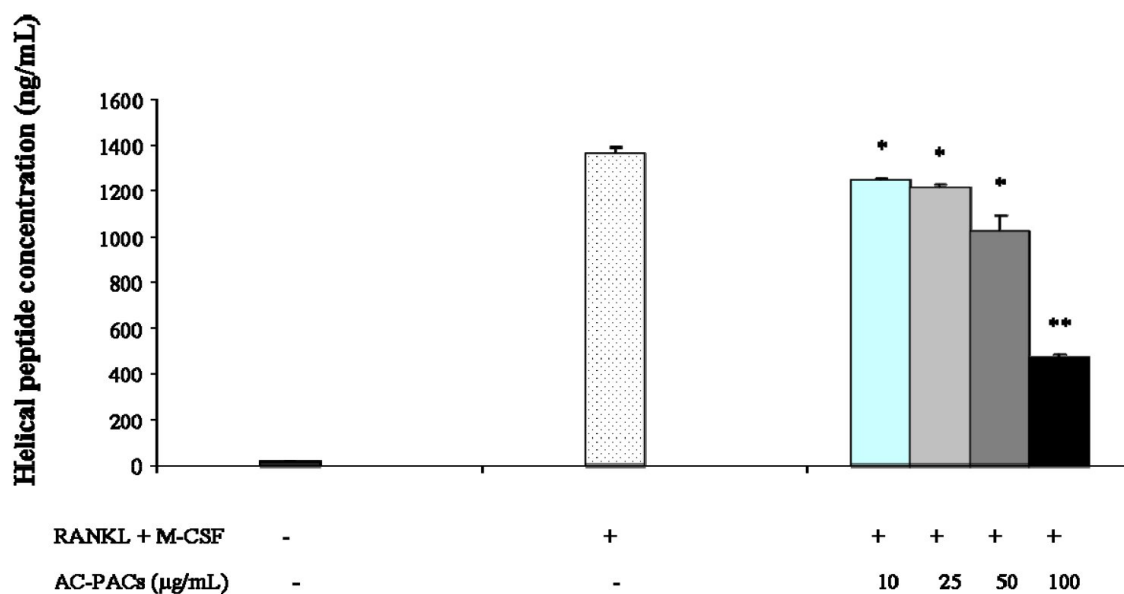
Since the production of IL-8 by osteoclasts has been previously indicated as one of the steps of the signalling pathway for the recruitment of cells involved in bone remodelling [15], the demonstrated effect of AC-PACs on the secretion of this cytokine confirms the potential of these molecules to play a role in the regulation mechanisms of bone destruction. Gelatinases (MMP-2 and -9) derived from both resident and inflammatory cells participate in the pathological destruction of connective tissue. Accordingly, the important decrease of the secretion of both proteinases can be a quite valuable

outcome regarding the control of connective tissue destruction mediated by such host-derived enzymes in the context of periodontal disease. Indeed, the AC-PACs were already shown to affect MMP-1 and -9 secretion by LPS-stimulated macrophages, which was attributed to a reduction on the phosphorylation of five intracellular kinases and the inhibition of nuclear factor-kappa B (NF- κ B) [7]. However, the exact mechanism by which AC-PACs inhibit MMP secretion still deserves further investigation.

2.5. Bone resorption

The quantification of collagen helical peptides was performed by an enzymatic immunoassay to investigate the effect of AC-PACs on bone resorption activity of osteoclasts. A significant decrease ($p < 0.05$) on the release of helical peptides from the bone matrix was observed when osteoclastic cells were treated with any of the tested concentrations of AC-PACs (Figure 5). More specifically, a $66 \pm 1\%$ inhibition was obtained with AC-PACs at 100 $\mu\text{g/mL}$. This result further confirms the inhibitory effect of AC-PACs on osteoclastic activity.

Figure 5. Effect of AC-PACs on bone resorption mediated by osteoclasts. * $p < 0.05$, ** $p < 0.01$.



3. Experimental

3.1. General

The MTT [3-(4,5-diethylthiazol-2-yl)-2,5-diphenyltetrazolium diphenyltetrazolium bromide] cell proliferation assay kit was purchased from Roche Diagnostics (Mannheim, Germany). The Human Poietics® osteoclast precursor cell system and OsteoAssay™ human bone plate were obtained from Lonza Inc. (Allendale, NJ, USA). The MicroVue helical peptide enzyme immunoassay kit was purchased from Quidel Corp. (San Diego, CA, USA), while the interleukin-8 (IL-8), MMP-2 and

MMP-9 ELISA kits were obtained from R&D Systems (Minneapolis, MN, USA). The Leukocyte Acid Phosphatase kit was supplied by Sigma Chemical Co. (St. Louis, MO, USA).

3.2. Preparation of A-type cranberry proanthocyanidins

Cranberry proanthocyanidins were isolated from cranberry fruit (*Vaccinium macrocarpon* Ait.) using solid-phase chromatography according to a well-established method for proanthocyanidin isolation [3]. Briefly, cranberry fruit was homogenized with 70% aqueous acetone, filtered and the pulp discarded. The collected extract was concentrated under reduced pressure to remove acetone. The cranberry extract was suspended in water, applied to a preconditioned C₁₈ solid phase chromatography column and washed with water to remove sugars, followed by acidified aqueous methanol to remove acids. The fats and waxes retained on the C₁₈ sorbent were discarded. The polyphenolic fraction containing anthocyanins, flavonol glycosides and proanthocyanidins (confirmed using reverse phase HPLC with diode array detection) was eluted with 100% methanol and dried under reduced pressure. This fraction was suspended in 50% EtOH, applied to a pre-conditioned Sephadex LH-20 column which was washed with 50% EtOH to remove low molecular weight anthocyanins and flavonol glycosides. Proanthocyanidins adsorbed to Sephadex LH-20 were eluted from the column with 70% aqueous acetone, and monitored using diode array detection at 280 nm. The absence of absorption at 360 nm and 450 nm confirmed that anthocyanins and flavonol glycosides were removed. Acetone was removed under reduced pressure and the resulting purified proanthocyanidin extract freeze-dried. Methods including ¹³C-NMR, electrospray mass spectrometry, matrix-assisted laser desorption/ionization time-of-flight mass spectrometry and acid catalyzed degradation with phloroglucinol have all been utilized to confirm the presence of A-type linkages and concentration of proanthocyanidins present in the extract [2,3,14].

3.3. Cytotoxicity

The cytotoxicity of AC-PACs was measured by the MTT assay according to the manufacturer's protocol. Cells were seeded in 96-well culture plates and treated with AC-PACs at 10, 25, 50 and 100 µg/mL for two days. The cells were then incubated with MTT for 4 h. This allowed the formation of formazan crystals, which were solubilised overnight at 37 °C and the optical absorbance was measured on a microplate reader (Model-680, Bio-Rad Laboratories, Mississauga, ON, Canada) at a wavelength of 550 nm and a reference wavelength of 650 nm. Cytotoxicity was quantified as the relative decrease in the absorbance compared with untreated control cells.

3.4. Osteoclast formation

The human osteoclast precursor cells used in this study originated from haematopoietic stem cells isolated from the human bone marrow. Cell culture was initiated according to the manufacturer's instructions. Upon thawing, cells were washed, suspended in Osteoclast Precursor Basal Medium (Lonza Inc.) containing 10% heat-inactivated fetal bovine serum, 2 mM L-glutamine, 100 units/mL of penicillin, 100 µg/mL of streptomycin, and supplemented with RANKL (66 ng/mL) and M-CSF (33 ng/mL). Cells were then seeded in 96-well plates (1 × 10³ cells/well in 200 µL). AC-PACs,

prepared in sterile distilled water, were added to the cells at final concentrations of 10, 25 or 50 $\mu\text{g/mL}$. Cells incubated in the absence of AC-PACs were used as positive controls and cells incubated without RANKL served as negative controls since no differentiation was expected. Culture microplates were incubated for six days in a humidified atmosphere containing 95% air and 5% CO_2 at 37 °C to allow differentiation of precursors into mature osteoclasts. As recommended by the manufacturer, no replacement of culture medium was performed during the incubation period. Mature osteoclast formation was estimated by staining cells with a Leukocyte Acid Phosphatase assay kit. Tartrate-resistant acid phosphatase (TRAP)-positive multinucleated cells were stained in dark-red and the number of stained cells was determined under the microscope (100 \times magnification). Duplicate counts of triplicate wells for each condition were performed, and the means \pm standard deviations (SD) were calculated.

3.5. Interleukin and matrix metalloproteinase secretion

Culture supernatants from osteoclast precursor cells treated with various concentrations of AC-PACs for six days were collected and analyzed for IL-8, MMP-2 and MMP-9 production by means of commercial ELISA kits. The absorbance was read using a microplate reader at 450 nm with the wavelength correction set at 550 nm. The rated sensitivities of the commercial ELISA kits were 31.2 pg/mL for IL-8, 47 pg/mL for MMP-2 and 310 pg/ml for MMP-9.

3.6. Bone resorption

Osteoclast precursor cells were differentiated in OsteoAssayTM human bone plates by the addition of RANKL (66 ng/mL) and M-CSF (33 ng/mL) followed by a four-day incubation. Thereafter, the culture medium was replaced by fresh medium containing AC-PACs at final concentrations of 10, 25, 50 or 100 $\mu\text{g/mL}$, and cells were further incubated for four days. Fresh medium without AC-PACs (but containing RANKL and M-CSF) was used as positive control (differentiated cells) and medium without RANKL (with M-CSF) served as negative control (non-differentiated cells). By the end of treatment periods, culture supernatants were collected and analyzed for the presence of helical peptide 620-633 released from the $\alpha 1$ chain of type I collagen, the substrate of OsteoAssayTM human bone plate, by using a MicroVue helical peptide EIA kit. The effect of AC-PACs on bone resorption mediated by differentiated osteoclasts was recorded as a decrease in the release of collagen helical peptide compared to untreated control cells.

3.7. Statistical analysis

Data were recorded as means \pm SD of triplicate samples. The statistical comparisons were performed using Student's t-test with Bonferroni correction. The level of significance was set at $p < 0.05$.

4. Conclusions

Our results support that naturally occurring proanthocyanidins, such as those from cranberry, have a valuable potential for therapeutic application in the treatment and prevention of bone loss related to

inflammatory disorders as the periodontal disease. It seems that these plant-derived compounds would be able to interfere in osteoclastic cell maturation and physiology as well as in the bone matrix itself. Given their high biocompatibility, such substances may be easily introduced as a dietary supplement, which enables a large-scale application.

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definitions consulting



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consulting

[kuh n-suhl-ting]

Spell Syllables

Synonyms Examples Word Origin

adjective

- employed or involved in giving professional advice to the public or to those practicing the profession:
a consulting physician.
- of, relating to, or used for consultation:
a physician's consulting room.

Origin of consulting

1790-1800

1790-1800; consult + -ing²

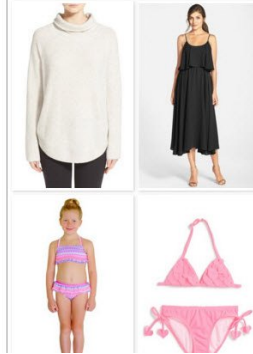
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Popularity: Bottom 40% of words

- 1 : providing professional or expert advice <a *consulting* architect>
- 2 : of or relating to *consultation* or a *consultant* <the *consulting* room of a psychiatrist>

First Known Use of CONSULTING

1801

1801

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Synonyms Examples Word Origin

noun

<http://dictionary.reference.com/browse/supplement>

1. something added to complete a thing, supply a deficiency, or reinforce or extend a whole.
2. a part added to a book, document, etc., to supply additional or later information, correct errors, or the like.
3. a part, usually of special character, issued as an additional feature of a newspaper or other periodical.
4. *Geometry*. the quantity by which an angle or an arc falls short of 180° or a semicircle.

verb (used with object)

5. to complete, add to, or extend by a supplement.

6. to form a supplement or addition to.

7. to supply (a deficiency).

Origin of supplement

English

(dictionary.reference.com/browse/Middle%20English)

Latin

(<http://dictionary.reference.com/browse/Latin>)

1350-1400

1350-1400; Middle English < Latin *supplēmentum* that by which anything is made full, equivalent to *sup-* *sup-* (<http://dictionary.reference.com/browse/sup->) + *plē-* (stem of *plēre* to fill; see *full* (<http://dictionary.reference.com/browse/full>)¹) + *-mentum* *-ment* (<http://dictionary.reference.com/browse/-ment>)

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unsupplemented, adjective

well-supplemented, adjective

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complement (<http://dictionary.reference.com/browse/complement>), **supplement** (see synonym study at complement (<http://dictionary.reference.com/browse/complement>))

Synonyms

2. addendum, epilogue, postscript. See appendix (<http://dictionary.reference.com/browse/appendix>). **5.** See complement (<http://dictionary.reference.com/browse/complement>).

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British Dictionary definitions for supplement

supplement

noun ('sʌplɪmənt)

1. an addition designed to complete, make up for a deficiency, etc
 2. a section appended to a publication to supply further information, correct errors, etc
 - 3 a magazine or section inserted into a newspaper or periodical such as one with colour
-

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Word Origin and History for supplement

n.

late 14c., from Latin *supplementum* "something added to supply a deficiency," from *supplere* (see *supply* (/browse/supply) (v.)).

v.

1829, from *supplement* (/browse/supplement) (n.). Related: *Supplemented*; *supplementing*.

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Definition of Supplement by Merriam-Webster

1. 2 : a part added to or issued as a continuation of a book or periodical to correct errors or make additions
2. 3 : an angle or arc that when added to a given angle or arc equals 180°

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Middle English, from Latin *supplementum*, from *supplēre* to fill up, complete — more at [supply](#)

First Known Use: 14th century

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