3,3'-diindolylmethane (DIM)

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3,3'-DIINDOLYLMETHANE (DIM) (PDF Version - 113 KB) This monograph is intended to serve as a guide to industry for the preparation of Product Licence Applications (PLAs) and labels for natural health product market authorization. It is not intended to be a comprehensive review of the medicinal ingredient. Notes Text in parentheses is additional optional information which can be included on the label at the applicant's discretion. The solidus (/) indicates that the terms and/or statements are synonymous. Either term or statement may be selected by the applicant on the label. Restrictions when this monograph is combined with other monographs (Class II and III applications): DIM cannot be combined with other monographed ingredients with estrogenic or anti-estrogenic effects as a Class II application (e.g., Soybean Extracts and Isolates, Indole-3-carbinol, Red clover isoflavone extract, Tribulus terrestris, Brassica oleracea varieties (cruciferous vegetables), Dong quai - Angelica sinensis). Theses products may be submitted as a Class III application. Date June 27, 2025 Proper name(s), Common name(s), Source information Table 1. Proper name(s), Common name(s), Source information Proper name(s) Common name(s) Source information Source ingredient(s) Source material(s) Part(s) Preparation(s) 3,3'-Diindolylmethane 3,3'-Methylenebis-1H-indole 3,3'-Diindolylmethane DIM N/A Brassica oleracea var. botrytis Brassica oleracea var. capitata Brassica oleracea var. gemmifera Brassica oleracea var. italica Whole plant Isolate 3,3'-Diindolylmethane N/A N/A Synthetic References: Proper names: NIH 2024; Common names: NIH 2024; Source information: Pradhan et al. 2005; Jongen 1996; Kwon et al. 1994; Bradfield and Bjeldanes 1991. Route of administration Oral Dosage form(s) This monograph excludes foods or food-like dosage forms as indicated in the Compendium of Monographs Guidance Document. Acceptable dosage forms for oral use are indicated in the dosage form drop-down list of the web-based Product Licence Application form for Compendial applications. Use(s) or Purpose(s) Source of (an) antioxidant(s)/Provides (an) antioxidant(s) (Fowke et al. 2006; Reed et al. 2005; Herraiz et al. 2004). Source of (an) antioxidant(s)/Provides (an) antioxidant(s) that help(s) fight/protect (cell) against/reduce (the oxidative effect of/the oxidative damage caused by/cell damage caused by) free radicals (Fowke et al. 2006; Reed et al. 2005; Herraiz et al. 2004). Helps to support/promote healthy estrogen metabolism/balance (Reed et al. 2005; Bell et al.2000; Wong et al. 1997; Bradlow et al. 1994). Helps reduce the severity and duration of symptoms associated with recurrent breast pain (cyclical mastalgia) (Reed et al. 2005; Zeligs et al. 2005). Note: If 3,3'-Diindolylmethane (DIM) is combined with other medicinal ingredients with antioxidant properties at Class II and III, there is an option to use the claim in plural. The singular should be used when the product only contains one chemical substance as the medicinal ingredient associated with this claim. Dose(s) Subpopulation(s) Adults 18 years and older Quantity(ies) Antioxidant Not to exceed 200 milligrams of DIM, per day (Laidlaw et al. 2010; Reed et al. 2008; Naik et al. 2006; Reed et al.2005; McAlindon et al. 2001; Bell et al. 2000; Wong et al. 1997; Bradlow et al. 1994). Healthy Estrogen Metabolism; Recurrent Breast Pain 60 - 200 milligrams of DIM, per day (Laidlaw et al. 2010; Reed et al. 2008; Naik et al. 2006; Reed et al. 2005; Zeligs et al. 2005; McAlindon et al. 2001; Bell et al. 2000; Wong et al. 1997; Bradlow et al. 1994). Direction(s) for use No statement required. Duration(s) of use No statement required. Risk information Caution(s) and warning(s) Products making healthy estrogen balance/metabolism claim Ask a health care practitioner/health care provider/health care professional/doctor/physician before use to exclude the diagnosis of a serious cause of hormonal imbalance (UpToDate 2024). Recurrent breast pain Ask a health care practitioner/health care provider/health care professional/doctor/physician if symptoms persist or worsen. Products providing 6 milligrams or more of DIM, per day Ask a health care practitioner/health care provider/health care professional/doctor/physician before use if you are taking medications or natural health products (Linus Pauling Institute 2017; Brinker 2010; Reed et al. 2005; Bradlow et al. 1994). Ask a health care practitioner/health care provider/health care professional/doctor/physician before use if you are attempting to conceive (Bennetts et al. 2008; Michnovicz et al. 1997). Stop use and ask a health care practitioner/health care provider/health care professional/doctor/physician if you develop liver-related symptoms (e.g., yellowing of the eyes and/or skin, dark urine, abdominal pain, jaundice) or symptoms of low estrogen (Reed et al. 2005; Dalessandri et al. 2004; Bell et al. 2000; Michnovicz et al. 1997; Wong et al. 1997; Bradlow et al. 1994). Products providing 6 milligrams or more of DIM, per day All subpopulations or Female subpopulation only Ask a health care practitioner/health

care provider/health care professional/doctor/physician before use if you have a liver disorder or symptoms of low estrogen such as joint pain, mood changes, changes in libido, hot flashes, night sweats, vaginal dryness or irregular menstruations (Reed et al. 2005; Dalessandri et al. 2004; Bell et al. 2000; Michnovicz et al. 1997; Wong et al. 1997; Bradlow et al. 1994). Male subpopulation only Ask a health care practitioner/health care provider/health care professional/doctor/physician before use if you have a liver disorder or symptoms of low estrogen such as joint pain, mood changes or changes in libido (Reed et al. 2005; Dalessandri et al. 2004; Bell et al. 2000; Michnovicz et al. 1997; Wong et al. 1997; Bradlow et al. 1994). Contraindication(s) All products Do not use if you are pregnant or breastfeeding (Reed et al. 2006; Michnovicz et al.1997). Known adverse reaction(s) No statement required. Non-medicinal ingredients Must be chosen from the current Natural Health Products Ingredients Database (NHPID) and must meet the limitations outlined in the database. Storage conditions Must be established in accordance with the requirements described in the Natural Health Products Regulations. Specifications The finished product specifications must be established in accordance with the requirements described in the Natural and Non-prescription Health Products Directorate (NNHPD) Quality of Natural Health Products Guide. The medicinal ingredient must comply with the requirements outlined in the NHPID. EXAMPLE OF PRODUCT FACTS: Consult the Guidance Document, Labelling of Natural Health Products for more details. References cited Bell MC, Crowley-Nowick P, Bradlow HL, Sepkovic DW, Schmidt-Grimminger D, Howell P, Mayeaux EJ, Tucker A, Turbat-Herrea EA, Mathis JM. Placebo-Controlled Trial of Indole-3- Carbinol in the Treatment of CIN. Gynecological Oncology 2000;78:123-129. 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NIH 2024: National Institutes of Health. PubChem. Bethesda (MD): National Library of Medicine, US Department of Health & Human Services. [Accessed 2024 June 25]. Available from: https://pubchem.ncbi.nlm.nih.gov/ Pradhan PK, Dey S, Giri VS, Jaisankar P. InCl3-HMTA as a Methylene Donor: One-Pot Synthesis of Diindolylmethane (DIM) and Its Derivatives. Synthesis 2005;(11):1179-1782. Reed GA, Arneson DW, Putnam WC, Smith HJ, Gray JC, Sullivan DK, Mayo MS, Crowell JA, Hurwitz A. Single-dose and multiple-dose administration of indole-3-carbinol to women: pharmacokinetics based on 3,3'-diindolylmethane. Cancer Epidemiology, Biomarkers and Prevention 2006;15(12):2477-2481. Reed GA, Peterson KS, Smith HJ, Gray JC, Sullivan DK, Mayo MS, Crowell JA, Hurwitz A. A phase I study of indole-3-carbinol in women: tolerability and effects. Cancer Epidemiology, Biomarkers and Prevention 2005;14(8):1953-1960. Reed GA, Sunega JM, Sullivan DK, Gray JC, Mayo MS, Crowell JA, Hurwitz A. 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Wong GY, Bradlow L, Sepkovic D, Mehl S, Mailman J, Osborne M. Dose-ranging study of indole-3-carbinol for breast cancer prevention. Journal of Cellular Biochemistry Supplement 1997;28-29:111-116. Zeligs MA, Brownstone PK, Sharp ME, Westerlind K, Wilsom SM, Johs S. Managing cyclical mastalgia with absorbable diindolylmethane: A randomized, placebo controlled trials. Journal of the American Nutraceutical Association (JANA) 2005;8(1):10-20. References reviewed Aggarwal BB, Ichikawa H. Molecular targets and anticancer potential of indole-3-carbinol and its derivatives. Cell Cycle 2005;4:1201-1215. Aggarwal BB, Shishodia S. Molecular targets of dietary agents for prevention and therapy of cancer. Biochemical Pharmacology 2006;71:1397-1421. Anderton MJ, Manson MM, Verschoyle R, Gescher A, Steward WP, Williams ML, Mager DE. Physiological modeling of formulated and crystalline 3,3'-diindolylmethane pharmacokinetics following oral administration in mice. Drug Metabolism and Disposition 2004;32(6):632-638. Bradlow HL. Indole-3-carbinol as a chemoprotective agent in breast and prostate cancer. In vivo 2008;22:441-446. Castanon A, Tristram A, Mesher D, Powell N, Beer H, Ashman S, Rieck G, Fielder H, Fiander A, Sasieni P. Effect of diindolylmethane supplementation on low-grade cervical cytology abnormalities: double-blind, randomised, controlled trial. British Journal of Cancer 2012;106:45-52. Cavalieri E, Rogan E. Catechol quinones of estrogens in the initiation of breast, prostate, and other human cancers: keynote lecture Estrogens and Cancer. Bradlow HL and Carruba G (eds.). Annals of the New York Academy of Sciences 2006;1089:286-301. Cited In: Bradlow (2008). Chang YC, Riby J, Chang GH, Peng BC, Firestone G, Bjeldanes LF. Cytostatic and antiestrogenic effects of 2-(indole-3-ylmethyl)-3,3'-diindolylmethane, a major in vivo product of dietary indole-3-carbinol. Biochemical Pharmacology 1999;58:825-834. [Abstract only] ChEBI 2018: Chemical Entities of Biological Interest. [Accessed 2024 June 25]. Available from: http://www.ebi.ac.uk/chebi/advancedSearchFT.do?searchString=indole-3-carbinol&queryBean.stars=3&queryBean.stars=-1 Dashwood RH. 1998. Indole-3-carbinol: anticarcinogen or tumor promoter in brassica vegetables? Chemico-Biological Interactions 110(1-2):1-5. [Abstract only] Higdon JV, Delage B, Williams DE, Dashwood RH. Cruciferous Vegetables and Human Cancer Risk: Epidemiologic Evidence and Mechanistic Basis. Pharmacological Research 2007; 55(3):224-236. Kim YS, Milner JA. Targets for indole-3-carbinol in cancer prevention. Journal of Nutritional Biochemistry 2005;16:65-73. Komiyama M, Higuchi K, Noguchi H. Selective synthesis using cyclodextrins as catalysts. Preparation of 3-(hydroxymethyl)indole from indole and formaldehyde. Supramolecular Chemistry 1995;4(4):265-269. Michnovicz JJ. Increased estrogen 2-hydroxylation in obese women using oral indole-3- carbinol. International Journal of Obesity and Related Metabolic Disorders 1998;22:227-229. [Abstract only] Minich DM, Bland JS. A Review of the Clinical Efficacy and Safety of Cruciferous Vegetable Phytochemicals Nutrition Reviews 2007;65(6):259-267. [Abstract only] NCBI 2024: National Center for Biotechnology Information. [Accessed 2024 June 25]. Available from: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=3712&loc=ec_rcs NIH 2012: National Institutes of Health. [Accessed 2012 March 12]. Available from: http://chem.sis.nlm.nih.gov/chemidplus/ProxyServlet?objectHandle=DBMaint&actionHandle= default&nextPage=jsp/chemidlite/ResultScreen.jsp&TXTSUPERLISTID=0000700061 Rogan EG. The natural chemopreventive compound indole-3-carbinol: state of the science. In Vivo 2006;20:221-228. Rosen CA, Bryson PC. Indole-3-carbinol for recurrent respiratory papillomatosis: long- term results. Journal of Voice 2004;18:248-253. Rosen CA, Woodson GE, Thompson JW, Hengesteg AP, Bradlow HL. Preliminary results of the use of indole-3-carbinol for recurrent respiratory papillomatosis. Otolaryngology- Head and Neck Surgery 1998;118(6):810-815. Sarkar FH, Li Y. Indole-3-carbinol and prostate cancer. Journal of Nutrition 2004;134:3493S- 3498S. Verhoeven DT, Verhagen H, Goldbohm RA, van den Brandt PA, van Poppe. G. A review of mechanisms underlying anticarcinogenicity by brassica vegetables. Chemico-Biological Interactions 1997;103(2):79-129. [Abstract only] Yuan Gao-feng, Bo Sun, Jing Yuan, and Qiao-mei Wang. Effects of different cooking methods on health-promoting compounds of broccoli. Journal of Zhejiang University Science B 2009;10(8):580-588. [Abstract only] Report a problem on this page Date modified: 2019-03-01

DOSAGE FORM(S)

Acceptable dosage forms for oral use are indicated in the dosage form drop-down list of the web-based Product Licence Application form for Compendial applications.

RISK INFORMATION

Caution(s) and warning(s) Products making healthy estrogen balance/metabolism claim Ask a health care practitioner/health care provider/health care professional/doctor/physician before use to exclude the diagnosis of a serious cause of hormonal imbalance (UpToDate 2024). Recurrent breast pain Ask a health care practitioner/health care provider/health care professional/doctor/physician if symptoms persist or worsen. Products providing 6 milligrams or more of DIM, per day Ask a health care practitioner/health care provider/health care professional/doctor/physician before use if you are taking medications or natural health products (Linus Pauling Institute 2017; Brinker 2010; Reed et al. 2005; Bradlow et al. 1994).Ask a health care practitioner/health care provider/health care professional/doctor/physician before use if you are attempting to conceive (Bennetts et al. 2008; Michnovicz et al. 1997).Stop use and ask a health care practitioner/health care provider/health care professional/doctor/physician if you develop liver-related symptoms (e.g., yellowing of the eyes and/or skin, dark urine, abdominal pain, jaundice) or symptoms of low estrogen (Reed et al. 2005; Dalessandri et al. 2004; Bell et al. 2000; Michnovicz et al. 1997; Wong et al. 1997; Bradlow et al. 1994). Products providing 6 milligrams or more of DIM, per day All subpopulations or Female subpopulation only Ask a health care practitioner/health care provider/health care professional/doctor/physician before use if you have a liver disorder or symptoms of low estrogen such as joint pain, mood changes, changes in libido, hot flashes, night sweats, vaginal dryness or irregular menstruations (Reed et al. 2005; Dalessandri et al. 2004; Bell et al. 2000; Michnovicz et al. 1997; Wong et al. 1997; Bradlow et al. 1994). Male subpopulation only Ask a health care practitioner/health care provider/health care professional/doctor/physician before use if you have a liver disorder or symptoms of low estrogen such as joint pain, mood changes or changes in libido (Reed et al. 2005; Dalessandri et al. 2004; Bell et al. 2000; Michnovicz et al. 1997; Wong et al. 1997; Bradlow et al. 1994). Contraindication(s) All products Do not use if you are pregnant or breastfeeding (Reed et al. 2006; Michnovicz et al.1997). Known adverse reaction(s) No statement required.

NON-MEDICINAL INGREDIENTS

Must be chosen from the current Natural Health Products Ingredients Database (NHPID) and must meet the limitations outlined in the database.

STORAGE CONDITION(S)

Must be established in accordance with the requirements described in the Natural Health Products Regulations.

SPECIFICATIONS

The finished product specifications must be established in accordance with the requirements described in the Natural and Non-prescription Health Products Directorate (NNHPD) Quality of Natural Health Products Guide.The medicinal ingredient must comply with the requirements outlined in the NHPID.

REFERENCES

Route of administrationOral

	Common name(s)	Source information		

	Source material(s)	Part(s)	Preparation(s)	
e3,3'-Methylenebis-1H-indole	3,3'-Diindolylmethane	DIM	N/A	Brassica oleraceavar.botrytis	Brassica oleracea	Whole p
e	N/A	N/A	Synthetic	