doi.org/10.67099/ijbahr2026.2.2.6 Vol. 2 (2) 2026, 201-205

IJBAHR

DIETARY MicroRNAs IN CANCERS: UNRAVELING THEIR BENEFICIAL, DETRIMENTAL AND CONTROVERSIAL ROLES

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Abstract: Through food-origin microRNAs (miRNAs), the complex relationship between dietary components and cancer aetiology has shown an intriguing paradigm. The dualistic nature of diet-derived miRNAs in cancer biology is critically assessed in this publication, which divides them into "the good" (tumor-suppressive), "the bad" (oncogenic), and "the ugly" (controversial with inconsistent evidence). Bioactive dietary miRNAs derived from curcumin, glyceollins, resveratrol, cranberry proanthocyanidins, and other food sources have been shown to survive gastrointestinal digestion, enter the systemic circulation, and modulate mammalian gene expression by targeting tumour suppressors or oncogenes. Notable examples include curcumin-mediated down regulation of oncomiR-21 targeting PDCD4 and PTEN in colon and pancreatic cancers, while tumours-suppressive miR-34a reactivation via dietary compounds enhances apoptosis through Notch-1 inhibition. However, significant challenges persist, including methodological inconsistencies in miRNA detection, non-physiological experimental conditions, cross-species sequence homology complications, and contradictory findings regarding functional relevance in vivo. The "ugly" includes the ongoing disputes about the clinical translatability of these xenomiRs, as certain studies do not replicate the initial encouraging findings. This review supports the need for uniform analytical frameworks, thorough mechanistic studies on miRNA stability and delivery, and the incorporation of multi-omics strategies to distinguish authentic biological relevance from experimental artifacts. Grasping the intricate functions of food-derived miRNAs offers groundbreaking possibilities for creating dietary strategies and miRNA-focused treatments in personalized cancer care.

Key words: Cross-kingdom gene regulation; bioactive dietary components; oncomiR; tumour suppressor miRNAs; xenomiR; nutria epigenomics

Submitted: 06-08-2026, Revised: 16-11-2026, Accepted: 18-11-2026

INTRODUCTION

MicroRNAs (miRNAs) are a class of ~22 nucleotides long ribonucleic acid (RNA) sequences that have attracted a lot of attention in studies pertaining to both animals (humans) and plants alike (Chrupek *et al*., 2012; Vaidyanathan *et al*., 2016). What is more interesting in the present scenario is the fact that certain miRNAs have been demonstrated to be sensitive to physical activity and diet (Guller and Russell, 2010) which raises the probability of the influence of an altered metabolic response of certain diseases in humans (Davidsen *et al*., 1985). Evolutionary history also contributes crucial factors that influence the pathology of human diseases (Gluckman *et al*., 2011).

Findings and Discussion

We have investigated certain reported miRNAs which are also found in certain food substances and thus identified to be "food-origin miRNAs" for the scope of this short communication due to the availability of two (or, more) species in a food chain. We have classified these food-origin miRNAs into three categories- "the good", "the bad", and "the ugly" based on their potential effect dependent on the consumption by us. We then discussed why only certain food-origin miRNAs should be shortlisted for further analyses rather than a whole range of them.

Table 1 has information about the various miRNAs that are identified to be bioavailable in certain dietary components and the seed region of the same hsa-miRNA biologically affecting the function of genes and/or targets in us with regards to certain cancers. It is an established fact that miRNAs regulate the expression of genes by binding to the 3' untranslated region (UTR) of the mRNA sequence (Vaidyanathan *et al*., 2016; Gottwein *et al*., 2006), and it is the seed sequence of any miRNA which is essential for this binding (Nigita *et al*., 2016). It is also worth mentioning that miRNAs are unique as one may be able to regulate many mRNAs individually and contrarily, multiple miRNAs may target any one mRNA to create complex

dynamics of cooperative regulations (Macfarlane *et al*., 2010; Calin and Croce, 2006; Gavrilas *et al*., 2016; Momtazi *et al*., 2016).

In the field of medical and health science research, cancer research has been focused on seeking novel and innovative approaches to understand the otherwise complex carcinogenesis and tumorigenesis mechanisms, and to identify the potential targets for therapeutics. In recent and relevant cancer research, the role of microRNAs (miRNAs) has been attracted by many researchers (Smalarz *et al*., 2022). As mentioned above, the MiRNAs are small, non- coding molecules which play a critical role in the regulation of corresponding genes and have been implicated in a wide variety of biological and physiological processes, including the development and progression of various cancers. Currently, the food-origin MiRNAs have got great attention for scientific investigations to assessing the potential involvement in cancer development and progression (Bhaskaran and Mohan, 2014). In this study, the authors aimed to criticize the recently published scientific evidence around the involvement of food-origin miRNAs in cancer research. This piece of critical analysis and discussion revolves around the latest research published on cancer, purpose and significance, challenges and opportunities as well as prospects for potential research avenues in this particular field.

Food-origin miRNAs refer to the miRNAs present in dietary sources, such as fruits, vegetables, and other plant-based or animal-based food products. These miRNAs are thought to survive digestion and enter the systemic circulation, where they may interact with host cellular machinery and potentially modulate gene expression (Zhang *et al*., 2019). The concept of food-origin miRNAs acting as regulators of gene expression in humans has garnered substantial interest due to its potential implications in cancer development and other diseases (Reda El Sayed *et al*., 2021).

The involvement and presence of intact dietary miRNAs in the blood stream of experimental animals and human samples. It has been recently documented and demonstrated that plant miRNAs are absorbed from the gastrointestinal tract and transported to various organs in mice models (Sanchita *et al*., 2018). Similar to this, a sizable quantity of plant miRNAs were found in human plasma, which further implies their uptake and role in the systemic circulation (Chen *et al*., 2021). It has also been explored that the food-origin miRNAs have shown a functional impact on cancer during various in-vitro as well as in-vivo studies. Recent research has also reported that the food-origin miRNAs tend to regulate cancer-developing processes, including but not limited to cell proliferation, angiogenesis, and apoptosis. Liu *et al*. (2021) explored that the miRl 59a in plant samples suppressed the breast cancer cells growth by targeting the c-Myc oncogene. These kinds of research highlighted the potential possible role of food-origin miRNAs as modulators of biomedical pathways in various cancers.

Although conceptualizing the involvement of food-origin miRNAs in cancer research is exciting, there is a need to address a variety of challenges and limitations to warrant a reliable and reproducible research outcome. One of the great challenges is the identification and quantification of food-origin miRNAs in a highly complex biological sample. This poses a considerable obstacle in precisely and accurately detecting the presence of similar miRNA sequences across the different species (Condrat *et al*., 2020). Moreover, number of technical factors linked to collection of sample, processing, and methodology for the detection and identification can acquaint with various biases and confusing factors.

Lack of consistent and standardized strategies and approaches for assessing the functional impact of food-origin miRNAs has been found to be another limitation. Many in-vitro studies utilize non-physiological concentrations of miRNAs, which may not accurately reflect the vivo situation. Furthermore, the mechanisms of food-origin miRNA delivery mechanisms to target cells and their stability within the systemic circulation remain poorly understood (Ortiz-Quintero, 2020; Chang *et al*., 2021).

It has been found that there are controversies and conflicting evidence related to the role and impact of food-origin miRNAs in cancer research. A few studies have failed to reproduce the findings of early research, leading to disputes regarding the reliability and relevance of food- origin miRNAs in complex and variable biological systems. Witwer & Zhang (2017) critically analyses and reviewed the methodology and interpretation of several studies claiming the uptake and functional relevance of food-origin and dietary miRNAs. Similarly, the potential for cross-species miRNA transfer raises questions about the biological significance of food-origin miRNAs. It is unclear whether the presence of dietary miRNAs in circulation represents a functional interaction with human gene regulation or simply reflects non-specific uptake and degradation.

Future studies need to be focused on addressing the known and foreseen challenges and controversies. Standardizing the collection of samples, processing, and detection and identifying methodologies could be able to improve the validity, comparability and reproducibility of findings. Furthermore, research should be looking into exploring and investigating the mechanisms of uptake, transport, and stability of food-origin and dietary miRNAs to find out their functional relevance. Several larger-scale epidemiological studies would be needed to assess and review the possible and potential association between food- origin and dietary miRNA intake and risk of cancer development and progression in human subjects. Integration of modem research approaches, for example, genomics, metabolomics, proteomics, as well as transcriptomics would be able to provide an understanding of the role and impact of food-origin and dietary miRNAs on cancer-related mechanisms and pathways comprehensively

CONCLUSION

The concept of involvement of food-origin and diet-derived miRNAs in cancer research is attractive and exciting yet, this area of research is still in its preliminary phases, and a lot of questions are still unanswered. While initial evidence suggests a potential and possible role and impact of food-origin and

dietary miRNAs in cancer development and progression, however, this includes various legitimate and persistent inconsistencies and controversies. Further SMART (specific, measurable, accurate, reliable, and timely) research would be required to explain the otherwise complex and unclear biological and physiological mechanisms, which might help establish the valid, authentic and vigorous strategies and methodologies, and assess the clinical significance of food-origin and dietary miRNAs in the field of cancer research. This will also provide a promising advancement in the understanding of the biological and physiological mechanisms of cancer development and progression and possibly as well as potentially provide guidance towards identifying the novel targets for therapeutic interventions. among Medical Students.

Table 2: Association of Demographic Characteristics with Pain, Disability, and Agility

Diet	miRNA	Nature	Genes/ Targets	Cancers	Biological Effect	Ref
Curcumin (Essential Curcuminoid of Turmeric) [IO,II]	↓miR-21	Oncomi (Oncogenic)	PDCD4	Colon	Apoptosis	Muddulur *et al.*, 2011
			PTEN	Colon and Pancreatic	PTEN	Watanabe *et al.*, 2011
			K-Ras	Pancreatic	Cell cycle regulation and proliferation	Volinia *et al.*,2006
			PTEN, PDCD4 and Bel-2	Melanoma	Cell cycle regulation and proliferation	Yang *et al.*,2013
	↑miR-34a, ↑miR-34c	Tumor Suppressive	Notch-I	Colon	Apoptosis, cell proliferation	Roy *et al*., 2021
	□miR-27a	OncomiR	SpI, Sp3, Sp4, ZBTBsI 0	Colon	Cell growth, ang10genes1s, Inflammation	Noratto *et al.*, 2013 Gandhy *et al*., 2012
Glyceollins (Found in unproductive kinds of nodule in Soybean in reaction to Symbiotic contamination)	↓miR-2I	OncomiR	PTEN,PDCD 4, TIMP3,TIMPI	Melanoa, Colon and Pancreatic	Cell cycle regulation and Proliferation	
	↑miR-22	Tumor Suppressive	EVl-I, ERBB3, CDC25	Pancreatic	Cell cycle regulation, apoptosis, and DNA repair	Tilghman *et al*.,2013 Rhodes *et al*., 2012
	↑miR- 34a	Tumor Suppressive	Notch-I	Colon	Apoptosis, cell proliferation	
Resveratrol	↑miR-I6	Tumor Suppressive	BCL2	Leukaemia	Induce Apoptosis	Peng and Croce, 2016
(Found in the skins of Raspberries, Grapes, Mulberries, Blueberries, Cowberry, Senna) [20]	↑miR- 663	Tumor Suppressive	AP-1, LNCaP cells	Lung; Induces Castration-Resistant Prostate Cancer (CRPC) Transform at 10	Cell proliferation	Tili *et al*., 2010 Jiao *et al*., 2014 Zhang *et al*., 2016
	↓ miR- 155	OncomiR	FOX03 A	Breast, Colon and Lung	Metastasis Occurrences; Intrusiveness and recurrence of breast tumors	Mattiske *et al*., 2012
Eggs [18]	↑ miR- 181a, ↑ miR- 181b	Tumor Suppressive	BCL2Al , PML- RARa	ndometrial Carcinoma, Acute Promyelocytic Leukaemia	Cell development, progress10n, and metastasis	Noratto *et al*., 2013 Gandhy *et al*., 2012 Tilghman *et al*.,2013
Cranberry Proanthocyani din (C-PAC) (Obtained from Cranberries) [21]	↑ miR- 410, ↑ miR 520d-5p	Tumor Suppressive	JHADl, OE19, OE33,VEGFA, ERBB2	Esophageal, Endometrial and Lung	P53,ang10genes1s,T-cell activation and apoptosis	Rhodes *et al*., 2012
High Red Meat (HRM)	miRl 7-92	OncomiR	CDKNl A	Colorectal	Cell proliferation	Peng and Croce, 2016

REFERENCE

Bhaskaran M and M. Mohan (2014) MicroRNAs: History, Biogenesis, and Their Evolving Role in Animal Development and Disease. Vet. Pathol. 51, 759-574. doi.org/10.1177/0300985813502820

Calin, G.A. and C.M. Croce (2006) MicroRNA signatures in human cancers. *Nat Rev. Cancer*, 6, 857-866. doi: 10.1038/nrc1997

Chang S-H., Y-C. Su, M. Chang and J-A Chen (2021) MicroRNAs mediate precise control of spinal interneuron populations to exert delicate sensory-to-motor outputs. Elife 10:e63768. doi: 10.7554/eLife.63768

Chen Xi, L. L.iu, Q. Chu, S. Sun, Y. Wu, Z. Tong, W. Fang, M.P. Timko, L. Fan (2021) Large-scale identification of extracellular plant miRNAs in mammals implicates their dietary intake. PLoS One.;16, e0257878. doi: 10.1371/journal.pone.0257878

Chrupek M, H. Siipi and L. Martinelli (2012) Bio-objects as "boundary crawlers:" the case of microRNAs. *Croat. Med. J*., 53, 285-288. doi: 10.3325/cmj.2012.53.285.

Condrat C.E., D. C.Thompson, M.G. Barbu, O.L. Bugnar, A. Boboc, D Cretoiu, N. Suciu, S. M. Cretoiu and S.C. Voinea (2020) miRNAs as Biomarkers in Disease: Latest Findings Regarding Their Role in Diagnosis and Prognosis. *Cells.* 9, 276-307. doi: 10.3390/cells9020276

Davidsen P.K., I.J. Gallagher, J.W. Hartman, M.A. Tarnopolsky, F. Dela, J.W. Helge, J. A. Timmons and S.M. Phillips (1985) High responders to resistance exercise training demonstrate differential regulation of skeletal muscle microRNA expression. *J. Appl. Physiol*. 110, 309-317. doi: 10.1152/japplphysiol.00901.2010.

El Sayed S.R., J. Cristante, L. Guyon, J. Denis, O.Chabre and N. Cherradi (2021) MicroRNA Therapeutics in Cancer: Current Advances and Challenges. *Cancers (Basel)* 3, 2680-2707. doi: 10.3390/cancers13112680

Gandhy S.U., K. Kim, L. Larsen, R. J. Rosengren and S. Safe (2012) Curcumin and synthetic analogs induce reactive oxygen species and decreases specificity protein (Sp) transcription factors by targeting microRNAs. *BMC cancer* 12, 564-575. doi: 10.1186/1471-2407-12-564

Gavrilas L.I., C.Ionescu, O. Tudoran , C. Lisencu, O. Balacescu and D. Miere (2016) The Role of Bioactive Dietary Components in Modulating miRNA Expression in Colorectal Cancer. *Nutrients*, 8. 590-608. doi: 10.3390/nu8100590

Gluckman P.D., F.M. Low, T.Buklijas, M.A. Hanson and A.S. Beedle (2011) How evolutionary principles improve the understanding of human health and disease. *Evol. Appl*., 4, 249-263. doi: 10.1111/j.1752-4571.2010.00164.x

Gottwein, E., X. Cai and B.R. Cullen (2006) A Novel Assay for Viral MicroRNA Function Identifies a Single *J. Virol*., 80, 5321-5326. doi: 10.1128/JVI.02734-05

Guller I. and A.P. Russell (2010) MicroRNAs in skeletal muscle: their role and regulation in development, disease and function. *J. Physiol*., 588, 4075-4087. doi: 10.1113/jphysiol.2010.194175

Jiao L., Z. Deng, C. Xu, Y. Yu, Y. Li, C. Yang, J. Chen, Z. Liu, G. Huang, L-C Li and Y. Sun (2014) miR-663 induces castration-resistant prostate cancer transformation and predicts clinical recurrence. *J. Cell Physiol.* 229, 834-844. doi: 10.1002/jcp.24510

Liu, J., F. Wang, H. Song, Z. Weng, Y. Bao, Y. Fang, X.Tang and X. Shen (2021) Soybean-derived gma-miR159a alleviates colon tumorigenesis by suppressing TCF7/MYC in mice. *J. Nutr. Bioch*. 92, 108627. doi: 10.1016/j.jnutbio.2021.108627.

Lynn, F.C. (2009) Meta-regulation: microRNA regulation of glucose and lipid metabolism. *Trends Endocrinol. Metab*., 20, 452-459. doi: 10.1016/j.tem.2009.05.007

Macfarlane, L-A and P.R. Murphy (2010) MicroRNA: Biogenesis, Function and Role in Cancer. *Curr. Genomics*, 11, 537-561. doi: 10.2174/138920210793175895

Mattiske, S., R. J. Suetani, P.M. Neilsen and D.F. Callen (2012) The oncogenic role of miR-155 in breast cancer. *Cancer Epidemiol Biomarkers Prev.* 21, 1236-1243. doi: 10.1158/1055-9965.EPI-12-0173

Momtazi A. A., F. Shahabipour, S. Khatibi, T. P. Johnston, M. Pirro and A. Sahebkar (2016) Curcumin as a MicroRNA Regulator in Cancer: A Review. *Rev. Physiol. Biochem. Pharmacol*. 171,1-38. doi: 10.1007/112_2016_3

Mudduluru G., J.N. George-William, S. Muppala, I.A. Asangani, R. Kumarswamy, L. D. Nelson and Heike Allgayer (2011) Curcumin regulates miR-21 expression and inhibits invasion and metastasis in colorectal cancer.. *Biosci. Rep.*, 31,185-197. doi: 10.1042/BSR20100065

Nigita, G., M. Acunzo, G. Romano, D. Veneziano, A. Laganà, M. Vitiello, D. Wernicke, A. Ferro and C.M. Croce (2016) microRNA editing in seed region aligns with cellular changes in hypoxic conditions. *Nucleic Acids Res*., 44, 6298-6308. doi: 10.1093/nar/gkw532.

Noratto G.D., I. Jutooru, S. Safe, G. Angel-Morales and S.U. Mertens-Talcott (2013)The drug resistance suppression induced by curcuminoids in colon cancer SW-480 cells is mediated by reactive oxygen species-induced disruption of the microRNA-27a-ZBTB10-Sp axis. *Mol. Nutr. Food Res*. 57, 1638-1648. doi: 10.1002/mnfr.201200609.

Ortiz-Quintero, B. (2020) Extracellular MicroRNAs as Intercellular Mediators and Noninvasive Biomarkers of Cancer. *Cancers (Basel*). 12, 3455-3494.

doi: 10.3390/cancers12113455

Peng Y and C.M. Croce (2016) The role of MicroRNAs in human cancer Signal Transduct. Target Ther.1:15004. doi: 10.1038/sigtrans.2015.4.

Rhodes L.V., S.L. Tilghman, S.M. Boue, S. Wang, H. Khalili, S.E. Muir, M.R. Bratton, Q. Zhang, G. Wang, M.E. Burow and B.M. Collins-Burow (2012) Glyceollins as novel targeted therapeutic for the treatment of triple-negative breast cancer. *Oneal. Lett*. 3, 163-171. doi: 10.3892/ol.2011.460.

Roy S., E. Levi, A.P.N. Majumdar and F.H. Sarkar (2012) Expression of miR-34 is lost in colon cancer which can be re-expressed by a novel agent CDF. *J. Hematol. Oncol.* 5, 1756-8722. doi: 10.1186/1756-8722-5-58

Sanchita, R. Trivedi, M.H. Asif and P.K.Trivedi (2018) Dietary plant miRNAs as an augmented therapy: cross-kingdom gene regulation. *RNA Biol*., 15, 1433-1439. doi: 10.1080/15476286.2018.1551693

Smolarz B., A. Durczyński, H. Romanowicz, K. Szyłło and P. Hogendorf (2022) miRNAs in Cancer (Review of Literature). Int. J. Mol. Sci.23, 2805-2822. doi: 10.3390/ijms23052805.

Tilghman, S.L., L.V. Rhodes, M.R.Bratton, P. Carriere, L.C. Preyan, S.M. Boue, T.S.Vasaitis, J.A. McLachlan and M.E. Burow 2013) Phytoalexins, miRNAs and breast cancer: a review of phytochemical-mediated miRNA regulation in breast cancer. *J. Health Care Poor Underserved*, 24(1 Suppl), 36-46. doi: 10.1353/hpu.2013.0036.

Tili E., J-J Michaille, B. Adair, H. Alder, E. Limagne, C. Taccioli, M. Ferracin, D. Delmas, N.Latruffe and C.M. Croce (2010) Resveratrol decreases the levels of miR-155 by upregulating miR-663, a microRNA targeting JunB and JunD. *Carcinogenesis*, 31, 1561-1566. doi: 10.1093/carcin/bgq143.

Vaidyanathan, V., V. Krishnamoorthy, N. Karunasinghe, A. Jabed, R. Pallati, C. H-J Kao, A.Wang, G. Marlow and L.R. Ferguson(2016) Are We Eating Our Way to Prostate Cancer-A Hypothesis Based on the Evolution, Bioaccumulation, and Interspecific Transfer of miR-150. *Non-Coding RNA*, 2, 2. doi: 10.3390/ncrna2020002

Volin,ia S., G. A. Calin, C-G. Liu, S. Ambs, A. Cimmino, F. Petrocca, R. Visone, M. Iorio, C. Roldo, M. Ferracin, R.L. Prueitt, N. Yanaihara, G. Lanza, A. Scarpa, A.Vecchione, M. Negrini, C.C. Harris and C.M. Croce (2006) A microRNA expression signature of human solid tumors defines cancer gene targets. *Proc. Natl. Acad. Sci.*, 103, 2257-2261. doi: 10.1073/pnas.0510565103.

Watanabe, A., H, Tagawa, J, Yamashita, K, Teshima, M, Nara, K, Iwamoto, M, Kume, Y, Kameoka, N,Takahashi, T, Nakagawa, N, Shimizu and K. Sawada (2011) The role of microRNA-150 as a tumor suppressor in malignant lymphoma. *Leukemia*, 25, 1324-1334. doi: 10.1038/leu.2011.81.

Witwer, KW. and C-Y Zhang (2017) Diet-derived microRNAs: unicorn or silver bullet? *Genes Nutr*. 12, 15-24. doi: 10.1186/s12263-017-0564-4.

Yang, C.H., J. Yue, M. Sims and L.M. Pfeffer (2013) The curcumin analog EF24 targets NF-κB and miRNA-21, and has potent anticancer activity in vitro and in vivo. *PloS one*, 8, e71130.doi: 10.1371/journal.pone.0071130.

Zhang, L., T. Chen, Y. Yin, C-Y Zhang and Y-L Zhang (2019) Dietary microRNA-A Novel Functional Component of Food. *Adv. Nutr*. 10, 711-721. doi: 10.1093/advances/nmy127.

Zhang,Y., X. Xu, M. Zhang, X. Wang, X. Bai, H. Li, L. Kan, Y. Zhou, H. Niu and P. He (2016) MicroRNA-663a is downregulated in non-small cell lung cancer and inhibits proliferation and invasion by targeting JunD BMC cancer, 16,315-324, doi: 10.1186/s12885-016-2350-x.

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