MERIT RESEARCH JOURNALS
www.meritresearchjournals.org

Merit Research Journal of Medicine and Medical Sciences (ISSN: 2354-323X) Vol. 4(1) pp. xxx-xxx, January, 2016
Available online http://www.meritresearchjournals.org/mms/index.htm
Copyright © 2015 Merit Research Journals

Original Research Article

Traditional Food Habits and their Possible Relationship in Diseases of the Mouth: The Use of Paprika

Menicagli R[1]*, Duca M[2] and Rancoita P M V[3]

[1]Senior Research" Biomed "20060 MEDIGLIA

[2]Istituti Clinici Perfezionamento (I.C.P). Hospital Bassini Milan

[3]University "Vita E salute" Hospital San Raffaele Milan

***Corresponding Author's E-mail menicagli@libero.it telefono 02 90661201**

Abstract

This study aims to verify whether the paprika containing polyphenols can be dangerous to the oral cavity for their property to protein precipitation and if capsaicin another usual compound present in the spice can increases these effects. At three saliva samples provided by volunteers, they are added either increasing amounts of two types of paprika, to different capsaicin content, both in a sample only pure capsaicin. The results were statistically analyzed by the Fisher Exact Test (FET). The results of proteins precipitation are not statistically correlated with increased concentrations of type of both paprika, p≥0.05, but it shows a trend phenomenon with the same values. Test 1 maximum precipitation 23% (rho = 0.95, p-value = 0.083), test 2 maximum precipitation 23.1% (rho = 1, p-value = 0.061). The addition of capsaicin alone detects a statistical tendency to precipitation, maximum 13% for concentrations fifty times those found in two samples of paprika. Protein precipitation is still relevant and mainly due to the polyphenols contained in paprika; this phenomenon can be enhanced by capsaicin and provide possible chronic effects on oral mucosa, raising the question of possible abuse of the paprika

Key Words: Oral Cancer, Paprika, Protein, Salivary Mucin

INTRODUCTION

Paprika is a spice typical of Hungary, now frequently used around the world It is obtained by drying and then pulverizing the peppers, mainly the genus Capsicum, after removing the inner membrane and seeds in it that contain the greatest amount of capsaicin. The paprika can still be sweet or spicy depending on the kind of peppers used, which leads to a change in the final colour. Paprika contains many substances that are considered bearers of many beneficial effects to health and many of these aspects have been reported in a recent report (Final report of the safety assessment of Capsicum Annuum extract, Capsicuum Annuum fruit extract, Capsicuum Annuum resin, Capsicum Annuum fruit powder extract, Capsicuum Frutescens and capsaicin (2007). In particular the paprika contains capsaicin, in concentrations ranging between 0.001% and 0.01%, and polyphenolic compounds to the maximum extent of 7mg/g of product. Capsaicin is a chemical compound from the many medical properties has been employed but particularly in the control of various forms of pain. Of particular interest is the treatment of topical capsaicin on the inflammatory process and that of neurological origin. Capsaicin is a powerful agonist of TRPV1 (transient receptor potential vanilloid): these receptors are selective in the ionic release through membrane channels, mainly expressed at the neuronal level, but also in other types of tissue. This type of receptor is activated by multiple stimuli, endogenous and exogenous, such as chemicals (resinferatoxina, anandamide), mediators of the inflammatory processes, temperature ≥ 43 degrees, and acidity (pH ≤ 5.3). The pain receptors are proteins, which possess specific loci for the molecules efferent, in other words spatial conformations to let for example only the capsaicin. When one of these receptors capsaicin binds, it opens the channel that releases calcium ions (Ca ++ 2), in turn triggering the release of neurotransmitters, which send signals to the brain and are responsible for the typical sensation of local burning. Followed by a step of

analgesia which lasts in time, in which the pain fibbers become insensitive to nociceptive stimuli of any nature. The unresponsiveness to painful stimuli, not only due to receptor desensitization but in a more complex condition called "defunctionalisation" which consists of functional and structural changes of the nerve fibres (Anarud, 2011). Making them insensitive over time, in other words with capsaicin did not induce tolerance for it and, therefore, there is a type of inflammatory response in the body, This response can cause the throat to swell, and makes breathing difficult and also damage the intestinal tract. The first commercial products for topical use of capsaicin are available in several countries since 1980. In 2009, NGX-4010, under the name of Qutenza®, was approved in Europe for the treatment of neuropathic pain in non-diabetic patients and in the US for PHN. For its mild analgesic effect, very similar to other drugs, the high cost and the irritating effects, this drug is usable only in the event of failure of other drugs. In the various articles that appear in the report, they are also mentioned the latest acquisitions on the antioxidant properties of capsaicin as possible anticancer activity especially for the gastric tract. To complete the picture on the effects of paprika we must now consider another important component of it, or the polyphenols. This class of chemical compounds also has a considerable antioxidant activity: that is, they are capable of neutralizing free radicals, namely those molecules that formed as a result of an insult of a different kind (stress, radiation, smoke, pollutants, emotional and physical stress, chemical additives, viral and bacterial attacks) and which, being unstable, tend to react with other molecules, damaging them at various levels and accelerating the process of cellular aging. They have anti-inflammatory, act as inhibitors on acid cascade arachidonic acid and thus prevents the triggering of the whole series of reactions that lead to the onset of the inflammatory process Much more important seems to be the anticancer action: that is, protect the cells from the attack of the direct carcerogeni compounds going to alter their activation mechanism Therefore it is very important in the diet to ensure a comprehensive consumption of fresh vegetables and raw (numerous scientific studies show a strong correlation between the consumption of fresh vegetables and reduced incidence of some cancers) atherogenic action, reduces the development of atherosclerosis and diseases related to it (stroke, thrombosis and cardiovascular disease). Another important question concern the possible contraindication in health.

Recently, were analyzed, the effects of polyphenols, such as contained in green tea, and, in a much more elevated in betel. Salivary mucins that include MUC5B (gel-forming) and MUC7 (-not gelling agent) are among the main factors that make up the mucosal layer, a protective barrier in the oral cavity, and it is possible that food components can affect the ability of the same.

A compound diet, green tea, contains moderate amounts of polyphenols, sometimes expressed as epigallocatechin gallate (EGCG) equivalent, can significantly alter both the properties, both the polymer network of MUC5B and the monomeric MUC7, as has been verified using the technique of the "rate-zonal centrifugation", for the fraction MUC5B present in a sample of human saliva. A protein precipitation is a very problem in chewing betel, smooth and essentially daily habit for about 500 million people worldwide. Here the effects are much higher, and they reply, with an incidence of oral cancer in vast regions of Asia very high: indicates ASR (age standardization rate), for Papua New Guinea to 25.4 (Heather and Davies, 2014). The purpose of this study is therefore to revisit the role that the paprika, as a commercial product, and routinely used in the preparation of many foods, can have in the equilibrium of the physiological conditions of the oral cavity.

EXPERIMENTAL APPARATUS - METHODS

Two saliva samples were provided by male volunteers aged respectively 34 and 40 years, who were not smoking, not denounced cardiovascular disease and physical examination showed no visible alteration of the oral cavity, it inflammation of the gums.
The two samples of paprika are:
- Paprika sweet variety made by "workshop of flavours", Italy bright red content in capsaicin 0.001%;
-Paprika strong variety made by “workshop of flavours”, Italy, red -yellow, content of capsaicin 0.005%
Average content of polyphenols in both samples paprika = 2.5 mg /gr

The pure capsaicin, which comes in white crystals, is made by Lyphar Biothec Co. Ltd. "Lyphar Supply Top Quality Natural Capsaicin Powder".

Saliva samples after the addition of paprika and the capsaicin as such, were stirred for a minute, and then rested for twenty minutes, before withdrawing a quantity of the clear supernatant, on which is the total protein concentration is determined by a spectrophotometric method with the biuret test.
The results were statistically analyzed by the Fisher Exact Test.

RESULTS

For both samples of paprika added to the maximum amount of precipitated protein is about 23%.see table 1, and 2. In these conditions the ratio between the average content of polyphenols added 0. 3.2 mg (value extrapolated from literature that indicates in 2.5mg/ g, the medium concentration), and the amount of total protein present in saliva 9 mg, is equal to 0.036, (3.6%).

The use of pure capsaicin addition to saliva in very

Table 1. Test with paprika red (capsaicina =0.001%)

SALIVA cc	*pH*	*TOTAL PROTEINS mg/dl*	*PROTEINS IN SAMPLE mg*	*PAPRIKA SAMPLE mg*	*CAPSAICIN SAMPLE mg*	*PROTEINS IN SOLUTION mg*	*PROTEINS ADSORPTION %*
3	*7.2*	*300*	*9*	*50*	*0.005*	*290*	*3.4*
3	*7.2*	*300*	*9*	*70*	*0.007*	*280*	*6.7*
3	*7.2*	*300*	*9*	*90*	*0.009*	*261*	*13*
3	*7.2*	*300*	*9*	*100*	*0.01*	*248*	*17*
3	*7.2*	*300*	*9*	*130*	*0.13*	*236*	*23*

Table 2. Test with paprika red-yellow (capsaicina =0.005%)

SALIVA cc	pH	TOTAL PROTEINS mg/dl	PROTEINS IN SAMPLE mg	PAPRIKA IN SAMPLE mg	CAPSAICIN SAMPLE mg	PROTEINS IN SOLUTION mg	PROTEINS ADSORPTION mg
3	7.0	320	9.6	50	0.025	301	5.6
3	7.0	320	9.6	70	0.035	287	10.3
3	7.0	320	9.6	90	0.045	268	16.3
3	7.0	320	9.6	100	0.05	240	21.8
3	7.0	320	9.6	130	0.065	227	23.1

Table 3. Test with pure capsaicin

SALIVA cc	pH	PROTEINS IN SAMPLE mg/dL	PROTEINS IN SAMPLE mg	CAPSAICIN IN SAMPLE mg	PROTEINS IN SOLUTION mg	PROTEINS ADSORPTION %
3	7	300	9	0.10	288	4.2
3	7	300	9	0.35	284	5.3
3	7	300	9	0.5	276	8.0
3	7	300	9	0.7	268	10.6
3	7	300	9	1.5	259	13.0

Tabe 4. ASR incidence for oral cancer in Hungary

Year	Estimated number of new cancers (all ages)	Male	Female	Both sexes
2012		1093	431	1524
	ages < 65	785	246	1031
	ages >= 65	308	185	493
2015		1109	434	1543
	ages < 65	785	243	1028
	ages >= 65	324	191	515
	Demographic change	16	3	19
	ages < 65	-	-3	-3
	ages >= 65	16	6	22

GLOBOCAN 2012 (IARC) - 18.9.2015

high concentrations, up to fifty times higher than those contained in the average paprika, involves a maximum of protein precipitation by 13%, see table 3. In all three tests the correlation between the concentration of polyphenols and capsaicin in paprika and the results relating to the values of precipitation of the protein as a function of the amount of paprika are not statistically significant,$p \geq 0.05$. For the experiment with paprika Red type, (table1), the values in statistical analysis with Fisher Exact Test are: p-value ≥ 0.085, rho =0.95.In test with paprika Red Yellow type, p-value =0.065, rho= 1, and with the employ also pure capsaicin the results are p-value =0.125 and rho=

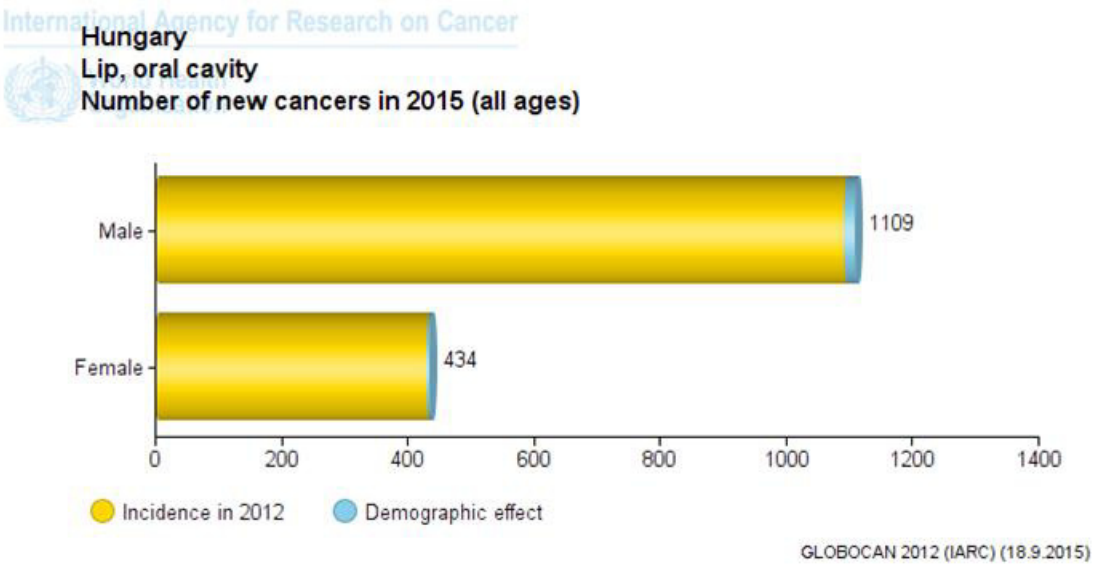

Figure 1. Hungary lip, oral cavity number of new cancers 2015

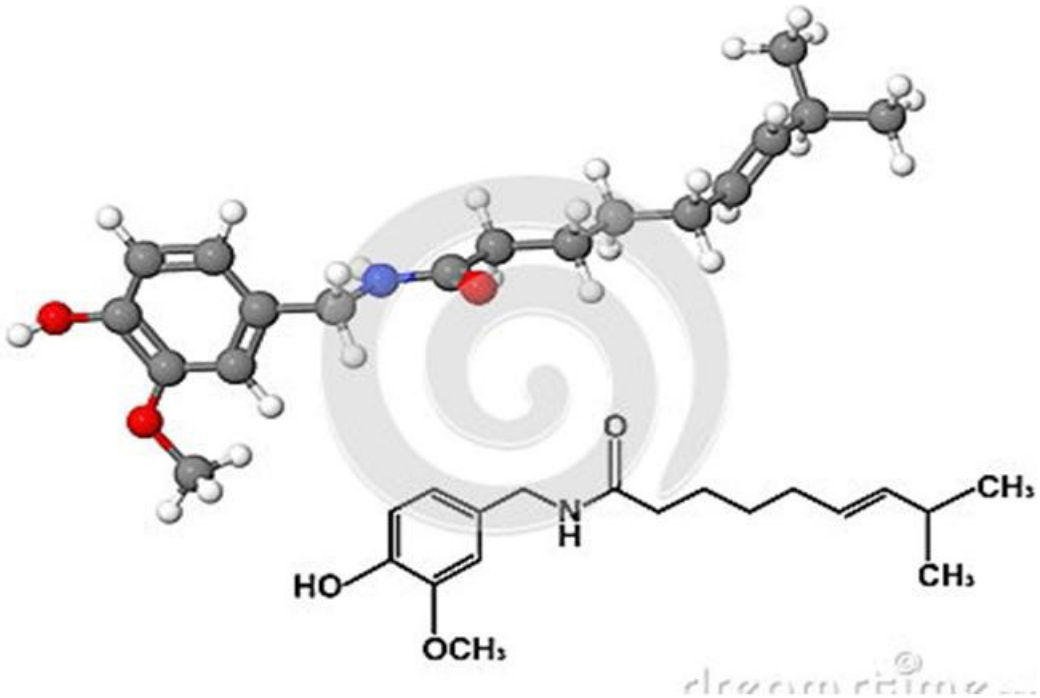

Figure 2. Capsaicin 3d structure

0.77.Theese statistics data, however, indicate a tendency to increases in the phenomenon of the interaction proteins/paprika compounds

DISCUSSION

The experiments were conducted by simulating as far as possible a contact between a normal saliva production, produced during a meal period of 25-35 minutes (25 cc) and the equivalent weight of paprika ingested (about one gram) in a plate typical Hungarian cuisine such as goulash. In the experimental conditions at 3 cc of saliva analyzed, they were then added, about 130 mg of the spice as the maximum value. As can be seen from Tables 1 and 2, even changing type of paprika, the results of precipitation of total proteins, are very similar. Increasing the amount of spice addition to saliva, values

Figure 3. Protein precipitation with paprika

Figure 4. Casein cogulation with capsaicin

of the precipitated proteins increases but with values that are not statistically significant, p-value≥0.05 and that is closely correlated to the ratio paprika / precipitated proteins and coming in both tests to a maximum precipitation of 23 % for 130 mg of spice used. The result of this test is also visible in Figure 2 where the surnatante phase retains a strong colour reddish. These first two tests analyzed statistically, however, indicate that there is a "trend of precipitation" of the proteins, depending on the amount of paprika addition, (see results Fisher's Exact

Test. In any case the two experiments show that the addition of capsaicin, this two in the sample, in an amount five times greater, and a specific quality of paprika considered "spicy", in no way implies an increase in precipitation of the protein. This important result is confirmed by the saliva test number three, in which, the parameters analyzed, or pH and total concentration of proteins are super imposable to the samples of saliva 1. The capsaicin was, in fact, added in concentrations up to fifty times higher than its content as in the case of the sample of paprika number 1 (0.25 mg / 0.0025) .The maximum value of precipitation of proteins, 13%, it has for a quantity of capsaicin addition, (equal a1.5 mg capsaicin / 9mg total protein), ie with a ratio p / p = 0.17 (17%). It is noted that these concentrations of capsaicin, according to literature data, are not present in any of paprika product on the market. In fact, the paprika is produced by drying the pepper (Capsicum annuum and subspecies), after removing the inner white membrane and seeds in it, where there is the highest concentration of capsaicin. In any case, see the two samples used in this study; a change in the concentration of capsaicin is very variable, especially for products that come from different countries to weather conditions because it not only depend on the species of plant capsicum, is influenced by cultivation. In our study, it is still detectable for each experimental condition made a modest capacity of union protein. Its absolute value is derived from the comparison of data on the amount of the precipitated proteins in test 2 (amount of capsaicin 0.065 mg), with that of the three tests, value pure capsaicin 00:10 mg). It can reasonably be assumed that in normal conditions of use of the paprika in food preparation now known, the sequestering power of the proteins by capsicin is not higher than 3%. This concentration value is given indirectly, as in this study was not isolated the adduct formed by complex proteins and polyphenols capsaicin, but it could however be considered to form a stable complex between the proteins and capsaicin itself through bond ionic. It has been demonstrated that the latter has power to interact with the lipophilic groups of the casein through the terminal aliphatic portion present in its structure, (Figure 1) In practice, if this situation the salivary imagine operating in the layer adhering to the oral mucosa, as is whether capsaicin acted as a lever between the mucins and the epithelium, with the aromatic part and methossilic facing receptors TRPV1, and that interacts with the aliphatic amino acids of type lipophilic salivary proteins. In the Figure 3 is well evident the clot that forms after the addition to milk, a small amount of capsaicin, and in the reality of everyday this phenomenon is reflected in the advice to drink milk every time you have the feeling of burning mouth after ingestion of hot spices based chili. The results obtained in this study indicate that, very likely, the promoters of the effect of precipitation of the protein, is a function of the presence of polyphenolic compounds present in paprika in considerable concentration compared to the values that can be found in other foods (egg: vegetables, spices, seeds, etc) and summarized in a recent review (Pérez-Jiménez et al., 2014). From the data of literature very deficient, (for the paprika as such only one reference) (Park et al., 2011), one can derive an average concentration of total polyphenols expressed in mg / gr ,between 1.5 and 4.0 with a maximum value of 7.0 mg / gr for a particular type of pepper from which it was prepared (Jeong et al., 2011; Mokhtar et al., 2015). These values compared with those expressed in above review, indicate how the paprika can be considered a source of polyphenols rather high whereas the use of spices that contain them in high quantities are limited in consumption. It 'very important in this regard to consider the attention and concern, reserved by the authors of the article, cited above (Heather and Davies, 2014), were are examined the process for reconsideration of all the networking, concerning benefices use regular green tea .The authors , with a work of studying the biochemical and physical-colloidal very accurate, demonstrate how the polyphenols precipitate, salivary mucins, and in particular, the fraction, gel forcing MC5B, with concentrations of polyphenols is not well defined, but which have seen their average value in green tea, taken from literature certainly not exceed that used in the study proposed. A reflection on the dangers of eating foods, spices and the like that contain significant amounts of polyphenolic compounds, compared to the conditions of a operation of protective systems, mucous membranes, oral cavity, it is therefore a topic of other investigations. The data obtained in this study, are, in fact, very correlated, with those of a previous work (Menicagli and Duca, 2014) and which concerns the dangerousness of the consumption of betel, in the possible formation of carcinomas of the oral cavity and the visible effect of tannins on the tongue, and on all the mucous membranes is, in fact, clearly visible. In this study, with a ratio polyphenols added to samples of saliva, compared to the amount of total protein present in it, equal to 13%, (30 mg / 250 mg), complete precipitation is obtained, not only proteins but also of all corpuscular elements. In our case, with a ratio of 3.5%, and lower than the previous by about a quarter, it has a protein precipitation of 23%, given very indicative for the potential chronic effects related to daily habits, which may also lead to greater consumption of paprika.as is the case in Hungary and in all the other Balkan countries. In addition to these laboratory evidence, we cannot not take into account possible influences that capsaicin may have, at the same time, a decrease of mucosal defences, establishing a local inflammatory process .Animal experiments have demonstrated that the application of capsaicin oral mucosa leading to a neurogenic inflammation associated with increases in blood flow in the gingivomucosal tissues. In recent survey, it was measured stimulation dental and blood, in some patients in response to placing

of capsaicin to study whether vasodilatation axon reflex-mediated cross the midline of the maxilla. Vasoactive reactions were mapped by laser Doppler, with obvious (Hemppainen et al., 2003) unilateral stimulation of alveolar mucosa and gingiva and related inflammatory processes. Another important data, in this regard, are reported in a recent Hungarian study. These has shown that (Suba et al., 2009) Hungary is leader on both morbidity as to the mortality of oral cancer in Europe and that the mortality rate for cancers of the oral cavity has dramatically increased in the period 1975-2002, both for the male population is the female. The increase in the incidence of oral cancer in the two sexes, even in the absence of risk factors such as smoking and alcohol, suggests that there are other predisposing parameters (Veyl et al., 2015), identified according to some epidemiological studies, with the increase of diabetes. This hypothesis is confirmed by a study (Duca et al., 2015) published by the authors of this article, on a retrospective survey of the main risk factors in a sample of laryngectomees. In the same study, however, among other risk factors identified, there are those that can deteriorate qualitatively and / or quantitatively the mucosal layer precipitating the salivary mucin its principal components and between these polyphenols. In Table 4, and in the graph below represents the values of incidence of tumours lip and oral cancer in Hungary and the projection for the year 2015 (IARC REPORT, 2012).

CONCLUSIONS

This study established that salivary proteins may be precipitated from the paprika and more by its polyphenols, with a small contribution of capsaicin .In these conditions there is a decrease of structural defenses of the oral cavity, likely in conditions of supply continues, rich in paprika (in Hungary gets in all foods, even desserts), a state of chronic lack of which - quantitative salivary mucin .That involves the possibility of aggression to the oral mucosa of various physic-chemical agents organic, and also become an adjunct of other diseases such as diabetes and / or autoimmune diseases, in establishing processes can lead to the formation of cancer oral cavity. The above is of course a working hypothesis, to be verified, but to be taken seriously.

REFERENCES

Anarud P (2011).Topical capsaicin for pain management, therapeutic potential and mechanism of action of the new concentration capsaicin 8% patch.Br J.Anaesth, Oct,107(4):490-502

Derry S, Moore RA (2013). Topical capsaicin (high concentration) for chronic neuropathic pain in adults. Cochrane Database Syst Rev. Feb 28;2:CD007393

Derry S, Moore RA (2012). Topical capsaicin (low concentration) for chronic neuropathic pain in adults. Cochrane Database Syst Rev. Sep 12;9:CD010111

Duca M, Menicagli R, Rancoita PM (2015). Preliminary study on laryngectomees for application of a new questionnarie for predictive screening in oral and laryngeal cancer Frontiera ORL Year VI,N1,June-July,1-22

Final report of the safety assessment of Capsicum Annuum extract, Capsicuum Annuum fruit extract,Capsicuum Annuum resin, Capsicum Annuum fruit powder extract, Capsicuum Frutescens and capsaicin (2007). International, J. Toxicol. 26 (suppl.1),3.106

Heather S, Davies (2014). Reorganisation of the Salivary Mucin Network by Dietary Components: Insights from Green Tea Polyphenols Plose One. 2014; 9(9): e108372.

Kemppainen P, Avellan NL, Handwerker HO, Forster Differences between tooth stimulation and capsaicin-induced neurogenic vasodilatation in human gingiva.

J Dent Res. 2003 Apr;82(4):303-7 (2003). Difference between tooth stimulation and capsaicin induced neurogenic vasodilatation in human gengives.J.Dent.Res. April,82(4),303-307

IARC REPORT (2012). GLOBOCAN

J Pérez-Jiménez, V Neveu, F Vos and A Scalber (2014). European J. Clin. Nutr.

Jeong WY, Jin JS, Cho YA, Lee JH, Park S, Jeong SW, Kim YH, Lim CS, Abd El-Aty AM, Kim GS, Lee SJ, Shim JH, Shi (2011). Determination of polyphenols in three Capsicum annuum L. (bell pepper) varieties using high-performance liquid chromatography-tandem mass spectrometry: their contribution to overall antioxidant and anticancer activity.J Sep Sci. Nov;34(21):2967-74. doi: 10.1002/jssc.201100524. Epub 2011 Sep 6.

Menicagli R, Duca M (2014). Possibile correlazione tra carenza di mucina nella saliva e cancro del cavo orale. Da un'analisi di particolari abitudini alimentari in paesi del subcontinente asiatico una nuova ipotesi di lavoro Frontiera ORL anno v numero 2

Mokhtar M, Soukup J, Donato P, Cacciola F, Dugo P, Riazi A, Jandera P, Mondello (2015). Determination of the polyphenolic content of a Capsicum annuum L. extract by liquid chromatography coupled to photodiode array and mass spectrometry detection and evaluation of its biological activity J Sep Sci. Jan;38(2):171-8. doi: 10.1002/jssc.201400993. Epub 2014 Dec 9. Page 7

Park J, Kim S, Moon B (2011). Changes in carotenoids, ascorbic acids, and quality characteristics by the pickling of paprika (Capsicum annuum l.) cultivated in Korea. J Food Sci. Sep;76(7):C1075-80. doi: 10.1111/j.1750-3841.2011.02297.x. Epub 2011 Aug 5.

Robbins WR, Staats PS, Levine J, Fields HL, Allen RW, Campbell JN, Pappagallo M (1998). Treatment of Intractable Pain with Topical Large-Dose Capsaicin: Preliminary Report Anesth Analg;86:579-83.

Suba Z, Mihályi S, Takács D, Gyulai-Gaál S (2009). Oral cancer: morbus Hungaricus in the 21st century]. Fogorv Sz. 2009 Apr;102(2):63-

Veyl D et al., (2015). Change in the incidence of diabetes mellitus in oral cancer patients based on long-term comparative study.Fogorv.sz.Mar 108(1):9-12