## Plastic Bottles cause Cancer as reviewed

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#### **Abstract**

The chemical Bisphenol A (BPA) was first synthesized in 1891; in 1930 a study found that BPA mimics estrogen. Today bisphenol A (BPA) is manufactured in excess of six billion pounds per year. BPA is most commonly used as the building block of polycarbonate plastic for products such as baby bottles and water bottles, epoxy resins (coatings that line food containers), and white dental sealants. It is also an additive in other types of plastic used to make children's

BPA molecules are bound by "ester bonds" to form a polymer used to make polycarbonate plastic. As the building block of polycarbonate, BPA is the primary chemical in polycarbonate, and it does not exist in only trace amounts. While plastics are typically thought of as stable, scientists have known for many years that the chemical bond between BPA molecules is unstable. The bond is disrupted by heat and acidic or basic conditions that release BPA into food or beverages in contact with the plastics.

Now, there have been over one hundred studies that link BPA that can cause cancer and other health conditions in exposed people. Pregnant woman who absorb a common chemical from everyday plastic products such as water bottles and other containers could be putting their unborn children at a risk of developing cancer and other diseases when they reach adulthood. Animal studies found that exposure in the womb to Bisphenol A caused changes associated with obesity, cancer and diabetes.

This chemical is banned in Canada, some states in U.S, other European countries, in the last two decades, more and more breast cancer in Korea has been related to BPA. Now, breast cancer is ranked the leading cause of cancer in Korean woman.

تم اكتشاف الماده الكيمياويه البيسفينول أي في عام 1891, وفي عام 1930 وجدت الدراسه بان تاثير مادة البيسفينول

يشابه الاستروجين. اليوم ينتج البيسفينول أي بمقدار ستة بلايين باوند سنويا. البيسفينول اي يدخل في تركيبة البلاستيكية والذي يدخل في صناعة قناني الحليب للاطفال قناني الماء البلاستيكية المادة الطلائيه (لتغليف علب الطعام والشراب من الداخل حشوات الاسنان البيضاء, وكذلك يستعمل كماده اضافيه الى البلاستيك المستعمل في صناعة العاب الأطفال

تكون ذرات البيسفينول أي ملتصقه بواسطة (استر باوند) لتكوين ماده للبلاستيك, ولانها جزء من مكونات البوليكاربونايت, يكون البيسفينول عنصر اساسى في البوكاربونايت. ولا يتواجد بكميه بسيطه وبما ان الظن بان البلاستيك ماده غير متغيره فان العلماء ولسنوات عديده يعلمون بان المواد الكيمياويه اللاسقه في تركيبة البيسفينول أي هي غير مستقره, لكون الاصره التي بينهما تنفصل بالحراره والمواد الحامضيه والقاعديه التي تطلق البيسفينول أي الي الطعام او المرطبات التي تلامس البلاستيك ."

الان يوجد أكثر من مئة دراسة بحثيه بان البيسفينول أي يسبب السرطان ويسبب مشاكل صحية أخرى لمن يتعرض إليه. الحوامل عند تعرضهن الى المواد الكيمياويه من خلال استعمال قناني الماء البلاستيكية وعلب الطعام. فأنهن يعرضن أطفالهن

الخور من على حراسها المرطان وإمراض أخرى عند البلوغ. الغير مولودين لخطر السرطان وإمراض أخرى عند البلوغ. في دراسة أجريت على الحيوانات في رحم الام, حيث تم تعريضها الى البيسفينول أي, فوجد بان الاجنه عند البلوغ أصيبت بالسرطان السمنة والسكري.

بالشراعان, الصحت, والمستري. ان مادة البيسفينول اى من المواد الممنوع استعمالها في كندا, بعض الولايات المتحدة الامريكيه, ودول أوربيه أخرى في فترة العقدين الماضيين. ان استعمال البيسفينول اى على نطاق واسع سبب حالات مرضيه أكثر وأكثر بين النساء وخصوصاً ما حدث بين النساء الكوريات على سبيل المثال

#### Introduction



We live in a plastic world. It's hard to believe the substance only came on the scene about 150 years ago when Alexander Parkes, an Englishman, mixed collodion, camphor, and ethanol together. He exhibited his invention at the 1862 Great International Exhibit in London. Then in 1907 Leo Baekeland created an entirely synthetic plastic from phenol and formaldehyde (1). People began questioning what in the long chains of unpronounceable chemical filling our homes. What are our babies sucking on when we hand them a pacifier, bottle, or teething ring? Bisphenol A, a chemical used in polycarbonate plastic, including pipes, dental fillings, water bottles, canned food, and many food wrappers; has come under fire. Bisphenol A is a "xenoestrogen" a known endocrine disruptor. Numerous animal studies have found effects on fetuses and newborns exposed to it (2). Nearly everyone is exposed to it, because polycarbonate plastic breaks down over time and leaches BPA into our bodies. The Center for Disease Control (CDC) found detectable level of BPA in the urine of 93% of 400 urine samples from national adults they been tested (3).

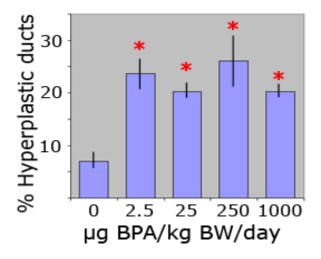
In 2007 experts agree that the average levels of BPA in people are above those known to cause harm to animals. More public concerned about BPA effects on our bodies (1). It is found that prenatal exposure to Bisphenol A causes breast cancer in adult rates (4). Prior work had shown that bisphenol A altered the growth of mammary tissues in ways that increase the risk of breast cancer and increase the sensitivity of breast tissue to cancer causing agents (4). Scientists have reported that around 95% of human adults tested positive for BPA. The chemical is similar to the female sex hormone, and has therefore been suspected of possible harm for years (5).

According to the Clean Air Council in United State of America (1); Americans uses 2.5 million plastic bottles every hours, add to that other countries uses disposable drinking bottles, baby bottles, food cans, teeth fixture which all made from Bisphenol A.

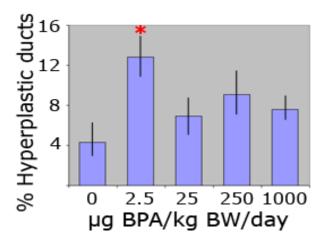
It is time to realize the danger of using this polycarbonated material and its serious impact on our bodies and our new generation. The important question is, do plastic bottles cause Cancer?

#### **Materials and Methods**

This study is related to effect of Bisphenol A on humans, also the effect of BPA on rats and mice. Murray et al (4) and his team in 2006 tested BPA effects on rats, which get breast cancer in much the same way as humans do. They (4), exposed pregnant female rats to a range of exposures of bisphenol A, from a 2.5  $\mu$ g/kg/day, to 1000  $\mu$ g/kg/day. Delivery was via a tiny pump implanted in the female. The research team tracked weights of the litters, and monitored time to puberty. Then at 50 days after birth, some of the females were sacrificed for histological examinations of mammary tissue. Another group was sacrificed at 95 days.



When Murray *et al* (4), examined the mammary tissue of 50-day old females microscopically, they found a 3-4 fold increase in ductal hyperplasias in all animals exposed to BPA (figure above). While all dosed animals had significantly more hyperplasias than controls, the treated animals did not differ from one another.



Amounts of BPA administered to the rats are reported in micrograms of BPA per kilogram of body weight per day. The incidence of breast cancer detected is presented as the percent of examined breast tissue ducts which were hyperplastic (that is, precancerous). Vertical black lines (called error bars) represent 5% confidence intervals (a measure of scatter among the data—95% of replicate experiments would be expected to fall within the ranges of the error bars. By day 95, the percentage of hyperplastic ducts had decreased, with only the lowest dose of BPA showing a statistically significant increase compared to controls. Non-monotonic dose response curves like this have been found regularly in work with BPA.

In animals treated with the two highest levels, 250 and 1000  $\mu$ g/kg/day, Murray *et al.* found cancerous lesions in the mammary glands. At 50 days of age, 25% of animals treated at those levels had CIS. This increased to 33% of animals by day 95.

When Murray  $et\ al\ (4)$ , examined the density of estrogen receptors in the animal's mammary ducts; they found the hyperplasic ducts had an increased number of cells that tested positively for estrogen receptor  $\alpha$ . This means that the cells were more sensitive to estrogen than those in the untreated animals. Histochemical analysis revealed higher rates of cell proliferation in the lesions. Both these tests are consistent with increased risk of breast cancer. They found no effect of exposure on weight or on time to puberty. Males exposed in the womb had smaller anogenital distances.

### **Results**

BPA is an unstable polycarbonate and is also lipophilic (fat- seeking), it can leach in to infant formula and other food products especially when heated (6). Once in food, BPA can move quickly in to people. BPA found in increased level in urine and/or blood samples taken from subjects who intentionally increased their intake of common food and drinks packaged in BPA (7, 8).

BPA has been found in blood (9), and urine (10) of pregnant woman and in breast milk soon after woman gave birth (11). BPA has also been found in blood samples from developing fetuses as well as the surrounding amniotic fluid(12), and it has been measured in placental tissue and umbilical cord blood at birth((13, 14), as well as in the urine of premature infants housed in neonatal ICUs (15).

Murray et al (4) reported that prenatal exposure to Bisphenol A causes breast cancer in adult rats. Prior work had shown that Bisphenol A altered the growth of mammary tissue in ways that increase the risk of breast cancer and increase the sensitivity of breast tissue to cancer causing agents.

BPA was administered in the diet of males and females rats and mice for 103 weeks resulted in carcinogenicity in male rats and mice and female rats. It is noted a slight increases in hematological malignancies in rats and male mice. In addition, a significant increases in testicular interstitial cell tumors was observed in male rats as well as a trend for an increase in fibro adenomas, a benign tumor of mammary gland, while the increase in testicular tumors was significant (16).

Components of numerous adult diseases, including cancer, may have their origins during fetal development when tissue architecture and homeostasis is established (17, 18, and 19). This is particularly evident for endocrine disruption which can lead to dysfunction of multiple target organs of sex steroids (20, 21). Of particular relevance for BPA are studies examining cancer risk following prenatal exposure to estrogens. Thus, exposure to exogenous estrogens during fetal and/or neonatal life can increase the incidence of various cancers. Consequently, it is imperative that the potential carcinogenic activity of BPA, an estrogenic compound, be assessed using fetal and early postnatal exposure protocols. This is further underscored by the clear presence of BPA in the plasma of newborn humans (0.2-9.2  $\mu$ g/ml) (22, 23).

The ability of BPA to influence cancer risk has been evaluated in three target organs: prostate, mammary gland, and uterus. These tissues have been the focus of significant attention because earlier studies have indicated that prenatal exposure to BPA as well as other estrogenic compounds led to altered morphology of sex steroid target organs (16).

During fetal life, alterations in normal prostate gland development can produce permanent changes that persist throughout adulthood and may increase the risk of disease in later life (24, 25). The

prostate differentiates from the cranial region of the urogenital sinus (UGS) (26). In humans, the first epithelial buds are observed in the lateral region of the UGS during the tenth week of pregnancy in a pattern that shows a remarkable similarity to that of bud development in mice and rats during the early phase of gland genesis (27).

During development, prostatic epithelial cells exhibit little androgen binding, and androgen receptor protein expression in epithelium is not required for differentiation (28, 29, and 30).

#### **Discussion**

BPA exposure comes from multiple sources. For example, BPA based polycarbonate is used as a plastic coating for teeth to prevent cavities, as coating in metal cans to prevent the metal from contact with food contents, and as the plastic in food containers, refrigerator shelving, baby bottles, returnable containers for juice, milk and water, micro-wave ovenware and eating utensils. BPA is unstable and it can leak to the food specially when heated (6), BPA can move quickly from the food to blood and urine (7, 8), in breast milk (11), in the undeveloped fetuses (12), in umbilical cord blood at birth (13, 14), also in the urine of premature infants housed in neonatal (15) that is way it is found in nearly every where in our bodies. Experiments on animals showed that a low concentration of BPA is carcinogenic.

The Environmental protection Agency has set a safe human intake dose from Bisphenol A is  $50\mu g/kg/day$  (31). In his study Murray et al (4) found that a much lower concentration can cause carcinogenic lesions in rats and mice in different area.

Based on existing evidence, I believe that BPA is associated with increased cancer in interstitial cell tumors of the testes. Early life exposure to BPA may induce pre-neoplastic lesions of the mammary gland and prostate gland in adult life.

Prenatal exposure to diverse and environmentally relevant doses of BPA alters mammary gland development in mice, increasing endpoints that are considered markers of breast cancer risk in humans.

#### **Conclusion**

BPA is a heavily produced industrial compound that has been detected in people worldwide, including more than 95 percent of 400 people in the United States (32). Studies have found BPA to be toxic at low doses (4), some similar to those found in people (16), yet not a single regulatory agency has updated safety standards to reflect this low-dose toxicity.

BPA is associated with a number of health problems and diseases that are on the rise in the U.S., Europe Korea and other parts of the world. Given widespread human exposure to BPA and hundreds of studies showing its effects on breast and prostate cancer and infertility

Yet despite its toxicity, BPA remains entirely without safety standards. It is allowed in unlimited amounts in consumer products, drinking water, and food, the top exposure source for most people. The lack of enforceable limits has resulted in widespread contamination of canned foods at levels that pose potential risks.

Consumer products, and is entirely without safety standards. BPA gives irrefutable proof that our system of public health protections must be strengthened to protect children and others most vulnerable to chemical harm.

((If BPA was treated as a drug, it would have been pulled immediately out of the market)) (33).

Growing children are particularly at risk to chemicals in their environment because they face greater exposure per pound of body weight and are physiologically more susceptible to them.(34) Children's exposures begin at conception, as chemicals, including BPA, cross the placenta in a pregnant woman's body (35) and can affect the embryo or fetus during critical periods of development. Even after birth, children's bodies remain immature, with underdeveloped detoxification mechanisms to protect them from BPA as well as drugs. Their brains and other

organ systems are constantly developing, undergoing periods of particular sensitivity to damage or disruption.

One the other hand, there are some reports minimizing the risk of BPA presence in drinking plastic (36). These few reports are prepared and monitored by big manufacturing companies of plastic drinking bottles. If we know that USA only produce 6 billion lb of BPA, we know why these companies are paying big money for such research to keep this product in the market.

BPA ranks in the top two percent of high production volume chemicals in the U.S., with annual production exceeding six billion pounds (4), and is so common in products and industrial waste that it pollutes not only people but also rivers, estuaries, sediment, house dust, and even air nearly everywhere it is tested. With high volume of production in the state and Europe, I wonder way this material is still on the market.

#### References

- 1-The Plastic World We Live In. If you've been following my blog, you've probably heard me dis on plastic at least a few times. The miracle product of the last century has..www.internationalorange.com/.../the-plastic-world-we-live-in/ United States CachedNAKED AGGRESSION PLASTIC WORLD LYRICS
- 2- Effects of Neonatal Exposure to Bisphenol A on Steroid Regulation ...by VL Bosquiazzo 2010
  Cited by 1 Related articles 1 Jan 2010 ... Abstract. Hormonally controlled vascular changes play a key role in endometrial development and in the differentiation process necessary for ...www.biolreprod.org/content/82/1/86.full
- 3-CALAFAT, A. M., YE, X., SILVA, M. J., KUKLENYIK, Z. and NEEDHAM, L. L.(2006), Human exposure assessment to environmental chemicals using biomonitoring. International Journal of Andrology, 29: 166–171. doi: 10.1111/j.1365-2605.2005.00570.x
- 4- Murray, TJ, MV. Maffini, AA Ucci, C Sonnenschein and AM. Soto. 2006. low level exposure in the womb to BPA causes breast cancer. Induction of mammary gland ductal hyperplasias and carcinoma in situ following fetal bisphenol A exposure. Reproductive Toxicology 23: 383-390
- 5-http://www.thedailygreen.com/going-green/latest/4592, Chemical in Baby Bottles, Other Plastics May Cause Cancer, Animal Studies Have Linked Bisphenol A to Harm During Pregnancy
- 6-Environmental Health Perspectives 103, Number 6, June 1995 ...by JA Brotons 1995 Cited by 546 Related articles Environmental Health Issues, bisphenol-A, food containers, lacquer coating, xenoestrogens, Environmental Health Perspectives 103, Number 6, June 1995: ... ehp.niehs.nih.gov/docs/1995/103-6/brotons.html
- 7- zaBilly Glenn Carwile (1935 2009) Find A Grave Memorial,12 Dec 2009 ... ROBERT LEE— Billy Glenn Carwile, 74, ...www.findagrave.com/cgi-bin/fg.cgi?page=gr&GRid=45348501
- 8- A new bill would ban BPA from all food and drink containers. ... common foods and drinks packaged in BPA-containing products (Carwile, 2009; Smith, 2009). ..www.breastcancerfund.org >
- 9-Histopathological Changes of Placenta Induced by Cyclophosphamide ...by R PADMANABHAN Rengasamy PADMANABHAN1, Shamer SINGH2. Article first published online: 2 MAY 2008. DOI: 10.1111/j.1741-4520.1984.tb00001.x ... onlinelibrary.wiley.com >
  - 10- Variability and Predictors of Urinary Bisphenol A Concentrations ...by Ye et al. 2008). Women from lower social classes in the United States .... 2009. Bisphenol A levels in blood and urine in a Chinese
  - 11- Bisphenol A (BPA) in breast milk soon after women gave birth (Kuroto-Niwa, 2006). ... www.breastcancerfund.org

- 12- ZBrushCentral IKEZUKI, 7 posts 7 authors Last post: 24 Aug 2003Join Date: Dec 2002. Location: JAPAN. Posts: 180. Post IKEZUKI www.zbrushcentral.com
- 13-EWG Lab Tests Find BPA, Perchlorate in Newborn Umbilical Cords ...EWG Lab Tests Find BPA, Perchlorate in Newborn Umbilical Cords. Dec 07, 2009. eponline.com/.../2009/.../ewg-lab-tests-find-bpa-perchlorate-in-newborn-umbilical-cords.aspx
- 14- Parent Bisphenol A Accumulation in the Human Maternal-Fetal ...by G Schönfelder 2002 Cited by 212 -... Human umbilical cord blood from the same subjects was taken from the umbilical vein ...ehp03.niehs.nih.gov/.../2002/...A707schonfelder/schonfelder-full.html
  - 15-Exposure to Bisphenol A and Other Phenols in Neonatal Intensive ...by AM Calafat (Calafat et ..... infants to BPA. Environ Health Perspect. 2009 Apr; 117(4):A163. ..www.ncbi.nlm.nih.gov
- 16- An Evaluation of Evidence for the Carcinogenic Activity of Bisphenol A, Ruth A. Keri,1 Shuk-Mei Ho,2 Patricia A. Hunt,3 Karen E. Knudsen,4 Ana M. Soto,5 and Gail S. Prins6
- 17- Dashed arrows link the observed effects at E18 with effects of prenatal BPA exposure observed during puberty and adulthood. 14 C. Sonnenschein et al. Page 7. ... BioEssays. 2004; 26, 1097–1107. 24. Baker SG, Cappuccio A, Potter JD.,
- 18-RA Keri, SM Ho, PA Hunt, KE Knudsen... Reproductive ..., 2007 Elsevier ... intervention. Wetherill et al. observed ... human exposure. These outcomes underscore the need for further study of the effects of BPA on tumor progression and therapeutic efficacy. 3.3. Evidence for genotoxicity induced by bisphenol A.
- 19-RA Keri, SM Ho, PA Hunt, KE Knudsen... Reproductive ..., 2007 Elsevier... often do not follow a monotonic dose—response curve [3]. Thus, the lack of a carcinogenic effect of pre ... 3. Potential carcinogenic modes of action of bisphenol A. An accurate assessment of the carcinogenicity of BPA requires an understanding of its potential modes of action
- 20-TJ Murray, MV Maffini, AA Ucci... Reproductive ..., 2007 Elsevier... Among these compounds, bisphenol A (BPA) is receiving increased attention due to its ubiquitous presence in ... The leading edge and TEBs were localized and starting 400 µm from the ... The percentage of ductal hyperplasias is significantly increased in BPA exposed animals at .. Induction of mammary gland ductal hyperplasias and carcinoma in situ following fetal bisphenol A exposure
- 21-RA Keri, SM Ho, PA Hunt, KE Knudsen... Reproductive ..., 2007 Elsevier ... but studies aimed at evaluating the potential non-genomic actions of BPA may yield ... Evidence for promotion of tumorigenic progression and inhibition of therapeutic efficacy by bisphenol A. ...Strikingly, there is no effective treatment for recurrent tumors, which lead to patient death. ... An evaluation of evidence for the carcinogenic activity of bisphenol A
- 22- G Schönfelder, W Wittfoht, H Hopp... Environmental Health ..., 2002 ncbi.nlm.nih.gov. Many different structural classes of industrial chemicals released into the environment possess potential hormonal activity or may alter normal patterns of hormone effects. Toxic effects may be produced at very low doses by interaction at hormone receptors (Triendl 2001). Many ... Parent bisphenol A accumulation in the human maternal-fetal-placental unit.
- 23- J Cheng, H Dehghani, DJ Hoeppner, C Dash... Cell Stem Cell, 2008 Elsevier ... Similarly, a further hallmark of transcriptionally repressed genome regions, DNA methylation of cytidine (5meC) is also significantly reduced in ESCs compared to NPCs (Bibikova et al., 2006) (Figures S1C and S2). Elevated Global Transcription in ESCs. ... Global transcription in pluripotent embryonic stem cells
- 24-SM Ho, WY Tang, J Belmonte de Frausto... Cancer research, 2006 AACR ... SM. Ho and WY. ... 2006 American Association for Cancer Research. Prostate enlargement in mice due to fetal exposure to low doses of estradiol or diethylstilbestrol and opposite effects at high doses. Developmental exposure to estradiol and bisphenol A

- increases susceptibility to prostate carcinogenesis and epigenetically regulates phosphodiesterase type 4 ...
- 25- Y Ogura, K Ishii, H Kanda, M Kanai, K Arima... ..., 2007 Bisphenol A induces permanent squamous change in mouse prostatic epithelium
- 26-PC Marker, AA Donjacour, R Dahiya... Developmental biology, 2003 Elsevier ... Available online 11 January 2003. Abstract. The ... 2001). In humans, rare basal cells have been identified with high expression of  $\alpha 2\beta 1$ -integrin, a marker expressed by putative stem cells in other tissues (Collins et al., 2001).
- 27- P Waterhouse, JM Penninger, E Timms... Science, 1995 sciencemag.org, 0. Halevy et al., Science 267,1018 (1995);
- 28-R Bhatia-Gaur, AA Donjacour... Genes & ..., 1999 genesdev.cshlp.org ... For tissue recombination studies, rat urogenital sinus mesenchyme (17.5 dpc) and mouse urogenital sinus mesenchyme and epithelium (15.5 dpc) were obtained as described (Cunha and Donjacour 1987; Higgins et al. 1989). Roles for Nkx3. 1 in prostate development and cancer
- 29-GS Prins... Endocrinology, 1995 Endocrine Soc... 7227/95/\$03.00/O Endocrinology Copyright 0 1995 by The Endocrine Society Vol. 136, No. 3 Printed in USA The Developmental Pattern of Androgen Receptor Expression in Rat Prostate Lobes Is Altered after Neonatal Exposure to Estrogen
- 30- A Colombero, E Timms... Proceedings of the ..., 1999 National Acad Sciences ... Copyright © 1999, The National Academy of Sciences. ←: Lacey DL,; Timms E,; Tan HL,; Kelley MJ,; Dunstan CR,; Burgess T,; Elliott R,; Colombero A,; Elliott G,; Scully S,; et al. (1998) Cell 93:165–176, pmid:9568710.
- 31- Bette Hileman, 6 Dec 2006 ... According to Soto, a large body of previous research suggests bisphenol A might cause breast cancer. One study shows that the daughters of ...pubs.acs.org/cen/news/84/i50/8450bisphenol.html
- 32- R Siegel, E Ward, T Murray... CA: a cancer journal ..., 2007 Wiley Online Library
- 33-SM Ho, WY Tang, J Belmonte de Frausto... Cancer research, 2006 AACR There are increasing human health and wildlife concerns about low-dose estrogenic exposures because hormonally active xenoestrogens are ubiquitous in the environment (1). Bisphenol A
- 34-Pesticides in the Diets of Infants and Children COMMITTEE ON PESTICIDES IN THE DIETS OF INFANTS AND CHILDREN PHILIP J. LANDRIGAN, Chair, Mount Sinai School ...
- 35-O Takahashi 2000 Disposition of orally administered 2,2-Bis(4hydroxyphenyl) propane (Bisphenol A) in pregnant rats and the placental transfer to fetuses. ... <a href="https://www.ncbi.nlm.nih.gov/pubmed/11049811">www.ncbi.nlm.nih.gov/pubmed/11049811</a>
- 36- Wise GEER, safe plastic bottles, <u>www.wisegeek.com/is-it-bad-to-drink-water-from-plastic-bottles.htm</u>