



# The Adverse Effects of Estrogenic Pill Driven After Flexible Fertility on Environment in COVID-19 Situation

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## Abstract

The time comes now to really think about the national policy over contraceptive pill after COVID-19 mental depression. This planet might face an adverse effect on biodiversity after using such contraceptive pills. After preventing unwanted pregnancy, the consumed birth control pills pass from human to water system and start their undesirable second innings to suppress the fertility in aquatic lives, domestic or wild animals. Besides the aquatic lives, the presence of pill chemicals in urban and suburban water supplies can be boomeranged to innocent people. Thus, a considerable debate is raised in consequence on limit level concern but need to be stopped immediately to stop the infertility problem already, before COVID-19. In detail, steroidal estrogens at pollutant levels can develop breast cancer in women and prostate cancer in men. The steroidal estrogens at pollution level can suppress the growth of root flowering and germination. Ethinyl estradiol (EE2) is a synthetic estrogenic pill, which induces intersex in freshwater fish and caused significant drops in populations. It is the high time to retrospect the national policies on using the estrogenic pill.

**Keywords:** Estrogenic pill; Ethinyl estradiol; Synthetic hormones; COVID-19.

Received: 27 January 2021; Accepted: 19 February 2021.

Article type: Letter.

## 1. Introduction

Last year we witnessed COVID-19 pandemic which suppressed pollution in water<sup>[1,2]</sup> and air.<sup>[3,4]</sup> Despite the suppression in pollution level, health risk in COVID-19 period raised significantly for the air pollution sensitivity in human. This enhanced mortality in UK<sup>[5]</sup> US.<sup>[6,7]</sup> A little enhancement of nitrogen dioxide pollution enhances the spreadability of COVID-19 in Chinese cities.<sup>[8]</sup> Even though pollution level decreased, contamination in drinking water like PFAS, metals, or plasticizers raises respiratory symptoms,<sup>[9]</sup> cardiovascular and pulmonary diseases.<sup>[10]</sup> However, this COVID-19 in some cases enhanced the pollution in some special cases like medical waste, disinfectants, gloves, and mask.<sup>[11]</sup>

Unfortunately, there is no work conducted on the excessive use of the contraceptive pill in this pandemic time. This pandemic would drive several aquatic species towards extinction. The world needs an extensive study to aware politicians, environmental activists for preserving the biodiversity.

### 1.1 Pre-COVID-19 study of estrogenic pill on adverse effects

To scrutinize the purity of tap water, U.S. Geological Survey (USGS) tested the tap water for nine states and declared that 85 manmade chemicals like medications, birth control pills are slipped through water treatment system in 2008. According to USGS, such lower concentration can't be considered as a potential health threat at present. In contrary, researchers claimed that, the residual drugs at even an extreme dilution can destroy the fish, frogs and other aquatic species. Moreover, it has been proved that such a presence can impair human cell function as well.

In retrospection of contraceptive pollution for determining the threat intensity, the extensive use was revealed. In the UK only, more than 2.5 million women take contraceptive pills. The synthetic estrogenic pill ethinyl estradiol (EE2) is used commonly. Through urine, it comes to sewage systems and rivers, and can suppress sperm production in male fish along with several other harmful effects even at very low concentration. For envisaging the effect experimentally, researchers added EE2 in a Canadian lake to pollute the water at extremely low concentrations (5–6 ng•L<sup>-1</sup>; parts per trillion) level and found that the fish population reduced drastically and most strikingly, one species, the fathead minnow (*Pimephales promelas*),

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disappeared completely.<sup>[12]</sup> They conducted the research for consecutive 7 years at the Experimental Lakes Area (ELA) in northwestern Ontario, Canada and reported as Chronic exposure of EE2 to fathead minnow drove to the feminization of males by producing VTG mRNA and protein. On the other hand, excessive production of VTG in females in the normal breeding season, forced gonadal development. This makes the species extinct in the lake. Not only it is harmful for a short lifetime like fathead minnow, but on chronic exposure, it will affect similarly to other fishes, they are afraid. In 2014, a separate Family planning data for the USA served showed that 4.8 tones (1 ton = 1000 kg) of estrogenic contraceptive, equivalent to EE2.<sup>[13]</sup>

### 1.2. Importance of COVID-19 period study of estrogenic pill on biodiversity

Since COVID-19 started, the world is facing serial lockdowns and utmost social depression. The use of contraceptive pill broke all-time records and become unavailable in the market.<sup>[14,15]</sup> According to the UN, 47 million women might not avail of contraception, resulting in 7 million unplanned pregnancies if the lockdown continues for six months.<sup>[16]</sup> The highly populated country like India with developed pharmaceutical sector is also facing the same problem. In 2019, India, 1.8 million injectable contraceptive used and 41 million cycles of oral contraceptive pills, 2.5 million emergency contraceptive pills made available in the market. The demand reached in such an extent that 24 to 27 million couples are not getting such pills in this pandemic

time.<sup>[17,18]</sup> Indian pharmacy companies might produce such a huge amount of contraceptive very soon to tackle the situation. The situation is same for other countries.<sup>[19,20]</sup> This huge amount of contraceptive is getting released to the environment through urine which will put the bio-diversity under real threat.

### 1.3. Source of steroidal estrogens

About 7 billion population discharge natural steroidal estrogens (E1, E2, and E3) 30,000 kg/yr. and synthetic estrogen EE2 700 kg/yr. annually through birth control pill. Unfortunately, it does not end here. The total release of estrogenic waste is much higher in the scenario. US and EU discharge annual estrogen by livestock, 83,000 kg/yr., which is about double of human discharge. US animal farms discharged 49 tones of estrogen in 2002. Similarly, UK discharged 1315 kg estrone (E1) and 570 kg estradiol (E2) from the farm animal annually. In 2007, Kjær and his associates reported 68.1 ng/L of E1 in deep groundwater (Table 1), which is sufficiently close to drinking water to cause alarm.<sup>[21]</sup> The table shows the threat to us before starting COVID-19 pandemic in a very clear way.<sup>[22]</sup>

### 1.4. Chemistry of Estrogens

Estrogens are biologically active hormones that are derived from cholesterol and released by the adrenal cortex, testes, ovary and placenta in humans and animals. Some estrogenic compounds have also been found in plants.<sup>[23]</sup> Depending on source, basically they are classified as natural or synthetic

**Table 1.** The available data on the concentrations of estrogen before COVID-19 is shown here (in ng/L). The table shows dairy or swine farms add huge amount of estrogen in the environment.

Sample Type	E1	17 $\alpha$ -E2	17 $\beta$ -E2	E3	EE2
Lagoon pond	650	-	-	-	-
1 m deep groundwater	68.1	-	2.5	-	-
grazing land water	78	31	18	-	-
sea water	-	-	0.83	-	4.67
STP/effluent	12–196	6.4–12.6	6.2–42.2	-	0.59–5.6
treated cattle feedlots	720	1100	1250	-	-
biogas digestate	593	50	24	-	-
dairy farm waste water	370–2356	1750–3270	351–957	-	-
Sow urine	416–490	-	85–97	127–193	-
dairy pit slurry	2500–80,000	2000–5000	800–27,000	-	-
swine pit slurry	5900–150,000	4000–84,000	1800–49,000	-	-
swine manure	70	175	15	-	-
swine farm effluent	5200–5400	650–680	1000–1500	2200–3000	-
swine manure leachate	68.1	2.5	-	-	-

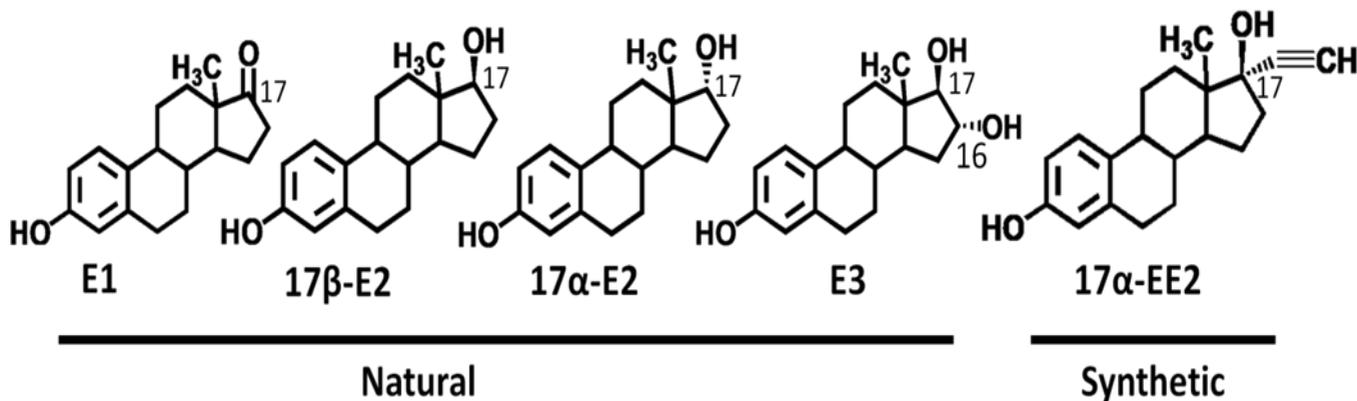


Fig. 1 Chemical structures of various estrogen hormones.

hormones and act as act as endocrine-disrupting chemicals (EDCs). Fig. 1 shows the common steroidal contraceptives like Estrone (E1), estradiol (E2), 17β-estradiol (17β-E2), 17α-estradiol (17α-E2) estriol (E3), ethinyl estradiol (EE2) are generally used nowadays (abbreviations are provided in parenthesis).

These steroidal estrogens (also known as the C18 steroidal group) comprised of one phenolic, two cyclohexane and one cyclo-pentane ring.<sup>[22]</sup>

1.5. Estrogen degradation and self-conversion

Degradation of estrogens depends upon the reaction condition of the local environment. Basically, it maintains

first-order kinetics and half-life varies in a few days. Their half-lives were calculated as 2 to 6 days in water and sediments. For 17β-E2 and E1 it varies from 0.2 to 9 days at 20 °C. Under ground water, in aerobic conditions, E2 takes only 10 days to decompose completely. However, synthetic contraceptive degrades from 1 to 0.62 μg/g per ten days. The half-life of EE2 is much higher (81 days in Australia) than the natural E2 under aerobic condition.<sup>[24]</sup> Under some aerobic conditions in lake sites of USA, the half-life was estimated for EE2 was 108 days, where no microbial biodegradation was observed. Schematically, here interconversions of estrogens are shown under various conditions (Fig. 2).

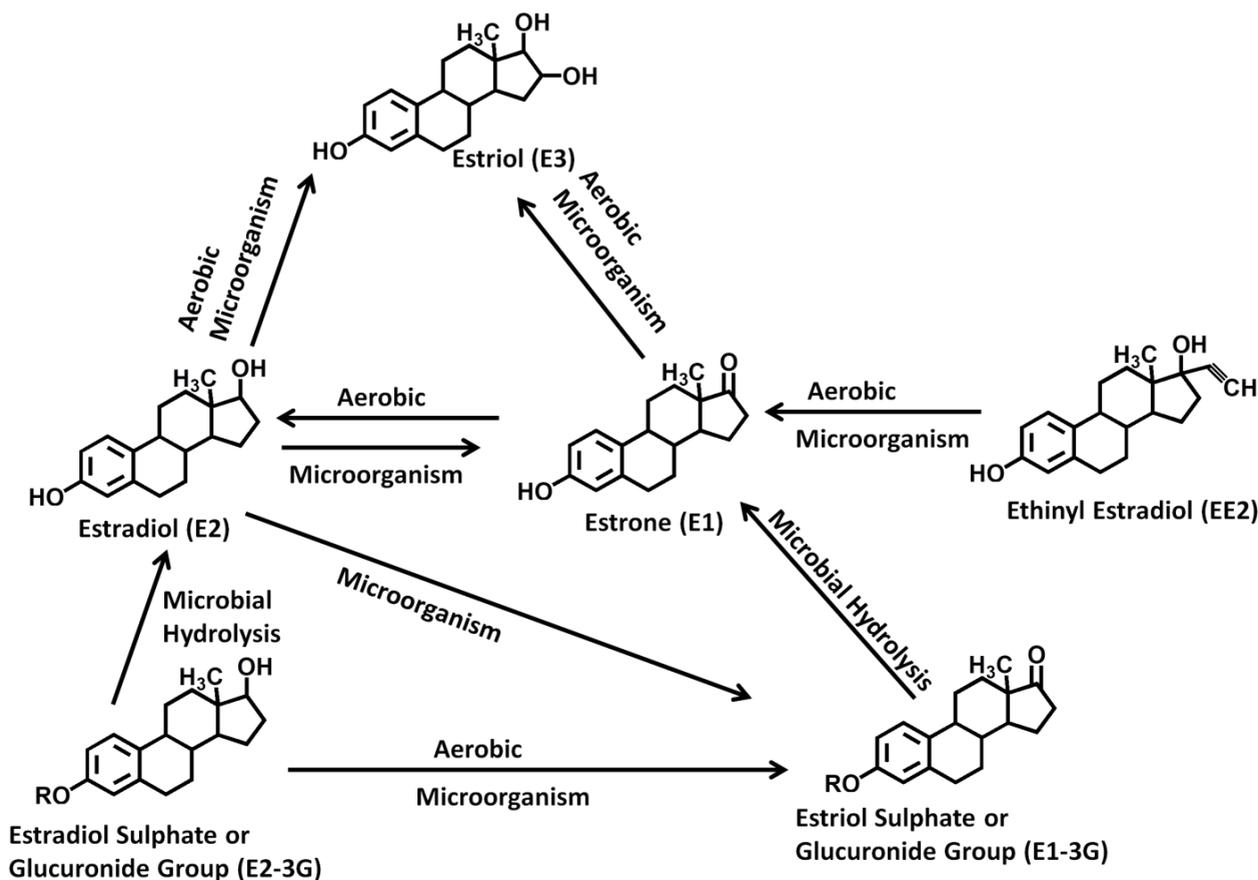


Fig. 2 Interconversion pathways of natural and synthetic estrogens is presented here schematically. The estrogens are getting oxidized and reduced under various natural conditions.

### 1.6. Cost calculation to protect environment

However, the actual situation is much more under threat, than we consider presently. In Britain, 50 sites have reached already 80% of noticeable EE2 levels at their water and with continual disposing of sewage, the aquatic lives will be disappeared very soon. Entire Europe is facing the same situation. In an emergency basis, EU proposed a 0.035ppt level for EE2 pollution in 2012 January for controlling the threat, but it is extremely expensive. Still the level is extremely higher than the experimental observation was found at Canadian lake against 5 parts per trillion! In 2012, UK based researchers Richard Owen and Susan Jobling published 'The hidden costs of flexible fertility' in Nature<sup>[25]</sup> and for a town of about 250,000 people, the installation of such water purifier will cost £10.3 million (100.1 crore Indian rupees), and it will take further £8000,000 (77.74 crore Indian rupees) additionally for running the purifier each year. So, for upgrading the 1,400-sewage waterworks, UK need to pay £30 billion (2,915,60 crore Indian rupees), which is completely impossible for a country for a single issue to handle with. The raised a very valid question, "are we willing to pay up or would we rather settle for environmental damage associated with flexible fertility?" Such huge cost rules out an immediate implication for their national water purification policy. Extracting the steroidal estrogens from water requires to be passed through active charcoal, which can't be implemented globally for higher coast and poor awareness. Although no links have yet been established yet on human health, it does not imply that it will remain innocent with increasing concentration in future.<sup>[26]</sup> Such a huge cost tells, once we face the problem behind bio-diversity, it would be apparently impossible to retrieve the environmental conditions as years ago.

### 1.7. Natural remedy

If the continuity in estrogen addition can be stopped, the aerobic oxidation, microorganism activity, photodegradation, accumulation by special plants can reduce the estrogen levels from environment effectively. For example, the most annoying EE2 when exhibiting the half-life of 108 days for degradation aerobic conditions without microorganism, it only takes under 23 h under sunlight for photodegradation.<sup>[27]</sup> Some plants also have some positive effect in reducing the estrogen from the environment. Several plants are generally employed for phytoremediation of toxic environments. So far a very few plants are reported to accumulate natural or synthetic like wetland macrophytes, leafy vegetables and algae together with poplar, maize and willow. In lab study, *Populus deltoides nigra* (wetland plant) and *Scirpus validus* (emergent wetland plant) can reduce the concentration of estrogens discussed here (17 $\beta$ -E2, E1, E3 and EE2) from solution. Like other plants, they of up-take such harmful threats through transport systems but not process nutrients here, instead sequester toxic substances in the plant vacuole. In such a unique method, they do this by accepting these estrogens through membrane bound pumps and carriers that usually take up nutrients that the plant needs. However, the detail mechanism is less clear so far. It may not be so

smooth for other trees always. In potato root growth and tuber size were reduced, where as the seedling growth was consistently inhibited in maize. In the case of tomato, the growth of root is also suppressed. It also has the negative effects of EE2 (at 7  $\mu$ m) on growth and photosynthesis in the green alga. Conversely, the estrogen suppressed lead-induced oxidative damage, DNA damage in wheat and also lowered endogenous H<sub>2</sub>O<sub>2</sub> levels. It attributes, natural healing speed would never be enough to preserve some animals normally in this pandemic condition.

### 2. Conclusion

If we do not control the use of estrogenic contraceptive immediately, it will control the existences of many species among us on the globe. Once it reaches to the aquatic system, it will be apparently impossible to remove it out for massive cost. The highly populated country like India if starts consuming contraceptive pills, it may wipe out aquatic lives deeply. We should ban it before witnessing any damage. The sperm count in west drastically reduced among men nearly halved per cent in just 40 years among men, temporal trends in sperm count: a systematic review and meta-regression analysis.<sup>[28,29]</sup> which might be associated with estrogen pollution along with other causes like pesticide pollution, alcohol, caffeine, processed meat, stress, smoking, obesity. Aquatic animal protein supply can be adversely affected without immediate major precaution. The time comes now to think the issues like biodiversity, aquatic lives, and infertility seriously before using Ethinyl estradiol (EE2), particularly in the pandemic situation.

### Acknowledgements

This work was supported by International Institute of Invincible Rhythms, Shimla, India, before joining NIMS, Japan.

### Supporting information

Not applicable

### Conflict of interest

There are no conflicts to declare.

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