

## THE CYTOTOXIC EFFECT OF RETINOID AND RETINOL ON PREGNANT WOMEN

Alaa Abduljabbar Abdulrazzaq<sup>1</sup>, Farah T.O. Al-Jumaili\*<sup>2</sup> and Noor A. Oohayyed<sup>2</sup>

<sup>1</sup>Department of Plant Biotechnology, College of Biotechnology, Al-Nahrain University, Baghdad, Iraq.

<sup>2</sup>Department of Molecular and Medical Biotechnology, College of Biotechnology, Al-Nahrain University, Baghdad, Iraq.

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**Corresponding Author: Farah T.O. Al-Jumaili**

Department of Molecular and Medical Biotechnology, College of Biotechnology, Al-Nahrain University, Baghdad, Iraq.

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### ABSTRACT

Retinol is a subtype of retinoid that is derived from Vitamin A. Unlike prescription retinoids, Over-the-counter retinol is available as a component of skin care products such as lotions, gels, serums, and creams. Retinol may boost the synthesis of collagen and elastin in the dermis, the skin's innermost layer, contributing to its pro-aging and anti-acne properties. The production of more collagen may smooth out wrinkles and fine lines in older skin. In addition to treating blemishes, retinol exfoliates the skin's surface by eliminating dirt, germs, and dead skin cells. Vitamin A, also referred to as retinol is an essential vitamin for daily human function that regulates the cellular growth of epithelial tissue. According to research too much vitamin A can affect how embryos develop and lead to teratogenesis or the development of birth defects in an embryo. Excessive vitamin A and retinoid use during pregnancy often results in fetuses with defects of the face, limbs, eyes, skull, and central nervous systems. Furthermore, retinoids, which are vitamin A derivatives, are frequently prescribed by medical professionals to treat a variety of skin disorders as well as carcinomas, the most prevalent type of cancer in humans.

**KEYWORDS:** Vitamin A; Retinol; central nervous system; RALDH; RAR.

### INTRODUCTION

Vitamin A is a group of substances that have vitamin A activity . The most significant of these compounds are the active metabolites all-transretinoic acid,9-cisretinoic acid, and retinal, as well as retinol, the precursor of the derivatives that are metabolically active.<sup>[1]</sup> The immune system, reproduction, cell differentiation and proliferation, and embryonic development all depend on retinoid function. Fetal retinoid syndrome is a set of congenital abnormalities, or birth defects, that can develop from a mother's use of retinoids throughout her pregnancy.<sup>[2]</sup> The amount of congenital abnormality risk associated with oral isotretinoin therapy is still unknown. The total malformation rates of liveborn infants from prospectively recorded pregnancies ranged from 5% to 20%. Retinoids, which are artificially produced synthetic forms of vitamin A, are used to treat a range of skin conditions known as dermatological disorders.<sup>[3]</sup> The

most well-known retinoid is isotretinoin, also known as Roaccutane or Accutane, one of its previous brand names. It is used to treat severe cystic acne. Despite being useful in treating acne, isotretinoin and its commercial brands can have teratogenic effects on a developing baby, increasing the risk of birth defects. For this reason, they should not be used during pregnancy.<sup>[4]</sup> The timing of exposure during pregnancy affects the spectrum and severity of related disorders. However, deformities of the skull and face (craniofacial region); abnormalities of the central nervous system (CNS); abnormalities of the heart; and/or extra physical findings can be considered typical traits.<sup>[5]</sup>

Renal, thymus, and parathyroid gland abnormalities are possible further defects. Dietarily derived retinol is transformed by the mammalian body and stored as retinyl esters in the liver.<sup>[6]</sup> Esters are chemical mixtures of alcohol and acids that have been condensed. These retinyl esters undergo hydrolysis, which is followed by a chemical conversion into retinol, which enters the bloodstream and is subsequently distributed throughout the body.<sup>[7]</sup> The retinol transportation method in human bloodstreams is achieved by the retinol's attachment to plasma retinol-binding proteins. Cells that require retinoic acid can convert retinol into retinoic acid, thanks to the two enzymes retinol dehydrogenases (ROLDH) and retinal dehydrogenases RALDH.<sup>[8]</sup> The first enzyme, ROLDH, transforms retinaldehyde from retinal. Retinaldehyde is converted to retinoic acid by the second enzyme, RALDH. Retinoids also come in different forms, including 4-oxo-RA, didehydo-RA, 9-cis-RA, and all-trans-RA. Retinalinic acid functions as a ligand in the nucleus of a cell by binding to a certain protein's location and triggering two families of transcriptional factors.<sup>[9]</sup>

#### The availability of vitamin A

Two forms of vitamin A can be found in food for humans: preformed vitamin A, which is made up of retinol and retinol ester and is derived from animal sources; and protamine A carotene, which is made up of beta-carotene, which is thought to be the most important type, and can be derived from plant sources.<sup>[10]</sup> Additional naturally occurring sources of vitamin A include breakfast cereal fortified with vitamin A, orange and yellow fruits and vegetables such as sweet potatoes, pumpkin, carrots, squash, red peppers, eggs, milk, cheese, and dark green leafy vegetables like broccoli and spinach. Finally, organ meats like liver and fatty liver contain vitamin A.<sup>[11]</sup>



Figure 1 (sources of vitamin A).

#### The reasons for insufficient vitamin A

Following are the important causes of vitamin A deficiency<sup>[12]</sup>:

- Limiting the intake of vegetables and animal products might lead to malnutrition.
- An excess of urine excretion results from a vitamin A deficiency.
- Mothers who decide without nursing their children put them at greater risk of vitamin A insufficiency since breast milk provides an adequate amount of vitamin A for a newborn.

**The retinoid and retinol genes**

These two families, which attach to genes that react to retinoic acid, are called retinoic acid receptors (RAR) and retinoid X receptors (RXR). Three types of RXR and three types of RARs exist. Research employing rat embryos grown in vitro has demonstrated that retinoids directly affect the embryo, resulting in aberrant development of those embryos.<sup>[13]</sup> The quantity of active retinoid that builds up over time (concentration-time relationship) throughout different stages of organ development has some effect on developing organs. The rate at which the placenta transfers retinoid from the pregnant woman to her embryos or fetuses, the rate at which the maternal intestine absorbs retinoid, the maternal retinoid metabolism, and the half-life of the retinoid in the maternal plasma are the factors that determine the amount of active retinoid in the embryo.<sup>[14]</sup> Because different animals have different embryonic tissues, different effects on developmental processes may happen even when exposed to the same amount of retinoid.

As a result, the effects of a single retinoid can change between species. Retinoic acid contributes to the regulation of embryonic development by inducing gene transcription at different locations throughout the embryo.<sup>[15]</sup> Only when the right receptors are present and the concentration of retinoic acid falls within the right range for the receptors will cells react to retinoic acid. Many pathologists and medical experts study how precisely retinoic acid concentrations are regulated since different quantities of the hormone activate different genes.<sup>[16]</sup> During the first few weeks of human embryonic development, in particular, the retinoid helps to express Hox genes. Hox genes control how the embryo's body plan develops. The human Hox gene count is thirty-eight.<sup>[17]</sup> The Hox gene malfunctions in embryos exposed to high levels of retinoic acid, which upsets the developing embryo's axial patterning, the genetic regulation of body shape. Certain bodily parts that, as was previously indicated, need to maintain precise quantities of retinoic acid are where retinoic acid synthesis takes place.<sup>[18]</sup> Teratogenic retinoids might affect these levels. Since the embryonic spinal cord, central nervous system, and spinal cord contain the enzymes necessary for retinoic acid synthesis and catabolism, these anomalies may lead to developmental issues.<sup>[19]</sup>

**The most important benefits of retinol for the skin: -**

- Retinol or vitamin A is an antioxidant, known to prevent free radicals that can lead to cell damage, and also helps reduce skin aging and treat acne.
- The benefits of retinol in the fight against dark spots, vitamin A creams help lighten dark spots caused by the sun, and increase skin radiance by increasing blood cell turnover, helping you to look dull or rough skin.
- Retinol and retinoic acid, two topical forms of vitamin A, reduce wrinkles and slow down the aging process. These components have the power to increase collagen synthesis. Wrinkles appear as tiny fissures in the skin when UV radiation damages collagen. Thus, retinol activates the cells that produce new collagen, fortify your skin, and fill in fine lines beneath the surface, giving the appearance of smoother skin.<sup>[20]</sup>



**Figure 2 (The effect of retinoid on skin).**

It's also important to note that retinol is a reasonably priced skincare product. It is one of the few skincare components with advantages supported by science, and the cost is very affordable. Put differently, you don't have to shell out hundreds of dollars for a high-quality retinol serum or moisturizer. There are lots that are reasonably priced.<sup>[21]</sup>

#### **The side effects of retinoid and retinol acid**

Retinoids are known for being harsh on the skin. In some cases, some redness, dryness, or peeling may appear. However, this is just the retinol doing its work and not something to panic about<sup>[22]</sup> Acids such as AHAs, BHAs, and PHAs should be used with caution when using retinol because they may conflict with the medication. Additionally, stay away from stacking retinoids and benzoyl peroxide together as they can neutralize each other's effects.<sup>[23]</sup>

#### **The risks of using retinol during pregnancy**

- ❖ Retinol usage is not recommended during pregnancy. Eat a diet high in foods that contain beta-carotene, which is a safe form of vitamin A that may be found in red, orange, and yellow veggies as well as dark leafy greens. Take prenatal vitamins as well. If retinoid use occurs during pregnancy, a child may grow physically and mentally due to fetal retinoid syndrome (FRS), which includes:
- ❖ Delayed growth before birth or during lactation
- ❖ Skull and face (craniofacial) abnormalities, including cleft palate and hypertelorism (eyes wide apart) Ears small and low, missing ears, hearing loss

- ❖ Central nervous system problems, such as hydrocephalus Developmental delay and learning difficulties, microcephaly.
- ❖ Heart abnormalities
- ❖ Problems with the kidneys, thymus and parathyroid glands.<sup>[24]</sup>

## CONCLUSION

We advise against consuming any retinoid-containing medications while pregnant due to the known dangers associated with oral retinoid use. It's unclear how much retinol use actually puts the fetus at risk. Therefore, you may replace the retinol in a lot of products that contain other chemicals when pregnant, like hyaluronic acid, glycolic acid, azelaic acid, and all-natural moisturizers.

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