MIKRO- VA NANOPLASTIKLAR – OZIQ-OVQAT MAHSULOTLARIDAGI KONTAMINANTLARNING IMMUN TIZIMGA TA’SIRI

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Annotatsiya

Ushbu maqolada mikro- va nanoplastiklarning (MP va NP) atrof-muhitda keng tarqalishi hamda ularning inson organizmiga, xususan immun tizimiga ta’siri tahlil qilingan. Tadqiqotlarda MP va NP oziq-ovqat mahsulotlari, ichimlik suvi va atmosfera orqali inson organizmiga kirishi, oshqozon-ichak tizimi, o‘pka va boshqa organlarda to‘planishi mumkinligi ko‘rsatilgan. Ushbu zarrachalar hujayra darajasida oksidlovchi stress, yallig‘lanish jarayonlari va immunoregulyatsiya buzilishlarini keltirib chiqarishi aniqlangan. MP va NP makrofaglar faolligini o‘zgartirishi, proyallig‘lanish sitokinlari (IL-1β, IL-6, TNF-α va boshqalar) ishlab chiqarilishini kuchaytirishi hamda immun tizimining turli signal yo‘llarini faollashtirishi mumkin. Eksperimental tadqiqotlar mikroplastiklarning ichak mikroflorasi tarkibini o‘zgartirishi, to‘qimalarda yallig‘lanish jarayonlarini kuchaytirishi va immun tizimi hujayralari faoliyatiga ta’sir ko‘rsatishini ko‘rsatadi. Shuningdek, MP va NP ning reproduktiv tizim va metabolik jarayonlarga ta’siri ham qayd etilgan. Natijalar mikro- va nanoplastiklarning organizmda aseptik surunkali yallig‘lanish rivojlanishiga olib kelishi mumkinligini ko‘rsatadi. Shu sababli ularning inson salomatligiga ta’sir mexanizmlarini chuqur o‘rganish va xavfsizlik bahosini aniqlash dolzarb ilmiy muammo hisoblanadi.

Kalit so‘zlar: Mikroplastiklar, nanoplastiklar, immun tizimi, yallig‘lanish, oksidlovchi stress, sitokinlar, oshqozon-ichak tizimi, jigar.

Dolzarbligi

Hozirgi kunda plastik mahsulotlardan keng foydalanish natijasida atrof-muhitda mikro- va nanoplastik zarrachalarining miqdori keskin ortib bormoqda. Ushbu zarrachalar tuproq, suv, atmosfera hamda oziq-ovqat mahsulotlari orqali inson organizmiga kirib borishi mumkin. So‘nggi ilmiy tadqiqotlar mikro- va nanoplastiklar oshqozon-ichak tizimi, jigar, o‘pka va boshqa organlarda to‘planishi, hujayra darajasida oksidlovchi stress, yallig‘lanish jarayonlari hamda immun tizimi faoliyatining buzilishiga olib kelishini ko‘rsatmoqda. Shuningdek, ular sitokinlar ishlab chiqarilishiga, immun hujayralar faoliyatiga va organizmning himoya reaksiyalariga ta’sir ko‘rsatishi aniqlangan. Mikro- va nanoplastiklarning inson salomatligiga uzoq muddatli ta’siri hali to‘liq o‘rganilmaganligi sababli ushbu muammoni chuqur tadqiq etish muhim ilmiy va tibbiy ahamiyatga ega. Shu bois mikro-

va nanoplastiklarning immun tizimga ta’sir mexanizmlarini o‘rganish hozirgi davrning dolzarb ilmiy masalalaridan biri hisoblanadi.

KIRISH

Hozirgi kunda plastik mahsulotlardan keng foydalanish natijasida atrof-muhitda mikro- va nanoplastik zarrachalar (MP va NP) keng tarqalgan[1,2]. Plastik – asosiy tarkibiy qismi polimer bo‘lgan material bo‘lib, u polietilen, polipropilen, polistiren, polivinilxlorid, polietilentereftalat va boshqa turdagi polimerlarni o‘z ichiga oladi[3]. Plastik atrof-muhitga sanoat yo‘li bilan (to‘qimachilik, kosmetika, maishiy kimyo mahsulotlarida) yoki tabiiy yo‘l bilan, ya’ni foto- va gidrolitik parchalanish, oksidlanish va biologik degradatsiya natijasida mayda zarrachalarga bo‘linishi orqali tushadi. Shu tariqa hosil bo‘lgan zarrachalar NP (≤0,1 μm), MP (<5 mm), mezoplastik (0,5–5 sm), makroplastik (5–50 sm) va megoplastik (>50 sm) shakllarida bo‘ladi[4]. MP esa mikrovaflolar, mikroplyonkalar va mikrogarnulalar sifatida tasniflanadi[5].

MP va NP tuproq, suv, havo va oziq-ovqat mahsulotlarida keng tarqalgan. Ular tuproqni plastik chiqindilarning noto‘g‘ri utilizatsiyasi, qishloq xo‘jaligi faoliyati va kanalizatsiya suvlari loyini qo‘llash orqali ifloslantiradi. Dengiz va okean suvlarida MP va NP qirg‘oq, sirt va tubda to‘planadi, hatto Arktika dengiz muziga ham yetib boradi. Shuningdek, MP va NP ichimlik suvi, shakar, tuz va pivo kabi oziq-ovqat mahsulotlarida mavjudligi aniqlangan[6].

Plastik inson salomatligi uchun xavf tug‘diradi: u nafaqat ishlab chiqarish jarayonida, balki atrof-muhitga tushganda ham toksik ta’sir ko‘rsatadi. MP va NP organizmga oziq-ovqat, suv, nafas olish va teri orqali kirishi mumkin. Shu bilan birga, ular hujayralarga kirib, immun tizimi va boshqa organlar faoliyatini o‘zgartirishi, surunkali aseptik yallig‘lanish va toksik stress hosil qilishi mumkin[7].

ASOSIY QISM

Hozirgi vaqtda NP uchun xalqaro miqyosda yagona aniqlik mavjud emas. Yevropa oziq-ovqat xavfsizligi agentligi (EFSA) NPni “tabiiy, tasodifiy yoki sun’iy material, tarkibida bog‘lanmagan yoki agregat/aglomerat shaklida zarrachalar mavjud bo‘lib, ularning 50% yoki undan ko‘pi 1–100 nm o‘lcham oralig‘ida” deb ta’riflaydi [8].

MP va NP tuproqda keng tarqalgan, jumladan qishloq xo‘jaligi maydonlari, bog‘lar, qirg‘oq zonalari, sanoat hududlari va vodiysimon zonalarda [9]. Tuproqning ifloslanishi asosan plastik chiqindilarni yetarlicha utilizatsiya qilmaslik va qadoqlash materiallari sababli yuz beradi. Shuningdek, qishloq xo‘jaligi faoliyati ham MP va NPni tuproqga kiritadi; asosiy manbalar plastik mulch ishlatish va chiqindi suvni maydonlarga qo‘llashdir [10, 11].

Dengiz muhitida plastik chiqindilar tubda, sathda va sohil bo`yida uchraydi. Plastik okeanlar, dengizlar va hatto Arktika dengiz muzligigacha yetadi [12, 13]. Hisob-kitoblarga ko‘ra, okean va dengizlardagi plastik ifloslanishning 80%

quruqlikdan keladi [14]. MP va NP shuningdek ichimlik suvi manbalarida, ko‘llar, daryolar, yerosti suvlarida ham uchraydi [15] va ichimlik suvlarida mavjud [16, 17]. Dengiz suvlaridagi MP va NP suv biologik resurslarini ham ifloslantiradi [18, 19].

MP va NPning asal, shakar, tuz, pivo kabi oziq-ovqat mahsulotlarida mavjudligi ham qayd etilgan [20–22]. Atmosferadagi MP va NP esa inson organizmiga zarrachalarning kirishining yana bir yo‘li hisoblanadi [23, 24].

Plastik inson salomatligi uchun hayotiy tsikli davomida har bir bosqichda xavf tug‘diradi: xomashyoni qazib olish va ishlab chiqarish jarayonida, maxsus qo‘shimchalar bilan boyitilishida, chiqindilar sifatida atrof-muhitga tushishida. Atrof-muhitdagi MP va NP ularning inson organizmiga oziq-ovqat, suv, nafas olish va teri orqali ta’sir qilishiga sabab bo‘ladi [2, 25].

Birinchi marta inson qonida MP mavjudligi haqida ma’lumotlar 2022-yilda University of Amsterdam Medical Center olimlari tomonidan taqdim etilgan [26]. 22 donor qoni namunalaridan 17 tasida 0,07 μm o‘lchamdagi plastik zarrachalari aniqlangan. Plastik zarrachalarning yarmi polietilentereftalatdan iborat bo‘lib, u butilka ishlab chiqarishda ishlatiladi; qon namunalarining 1/3 qismida polistiren zarrachalari mavjud, ba’zi namunalarida esa polietilen aniqlangan.

MP va NPning murakkab tarkibi va sirt xususiyatlari tufayli toksik moddalar va atrof-muhit patogenlari ularning sirtiga birikishi mumkin, shuning natijasida MP va NP og‘ir metallar, patogenlar va viruslarning tashuvchisi bo‘ladi, shuningdek, organizm oqsillari bilan bog‘lanadi [27, 28]. Natijada “korona” deb ataladigan murakkab tuzilma hosil bo‘ladi, bu MP va NPning yaxlitligini himoya qiladi. Bu esa ularning qon aylanishidagi yarim parchalanish davrini uzaytiradi, natijada hujayralar tomonidan so‘rilishi va toksik ta’siri kuchayadi.

Hayvonlar ustida olib borilgan tadqiqotlar shuni ko‘rsatdiki, oshqozon-ichak traktida (OIT) so‘rilgandan so‘ng MP va NP jigar, taloq, yurak, o‘pka, timus, reproduktiv organlar, buyraklar va hatto bosh miya – ya’ni gematoensefalik to‘siqni yengib o‘tib yetishi mumkin [29–31].

MP va NP toksikligini aniqlashdagi asosiy muammo ularning xususiyatlari va bio-mikromuhit o‘rtasidagi bog‘liqlikni o‘rganishdir. Ba’zi immun oqsillari MP va NPni aniqlab ularga birikadi; zarrachalarning o‘lchami va sirt zaryadi korona hosil bo‘lishiga ta’sir qiladi. Korona immunoglobulinlar, apolipoproteinlar, komplement oqsillari, yallig‘lanish oqsillari va qon ivish oqsillaridan iborat bo‘lishi mumkin [32–34]. MP va NP korona orqali hujayra retseptorlariga birikadi va korona oqsillari zarrachalarning hujayra ichiga kirishiga yordam beradi.

MP va NPning organlarga infiltratsiyasi zarrachalarning o‘lchami, sirt zaryadi, funksional xususiyatlari va ular duch keladigan substratlarga (oqsillar, uglevodlar, fosfolipidlar) bog‘liq [35]. MP va NPning hujayra membranasidan o‘tishi endotsitoz yoki zarrachalarning membrana kanallari va transport oqsillari bilan o‘zaro ta’sir orqali

sodir bo‘ladi [36]. Fagotsitoz, makropinositoz va klatrin/kaveola orqali endotsitoz kabi mexanizmlar mavjud. MP va NP zich hujayralararo kontaktlarni buzib, paratsellulyar translokatsiyani rag‘batlantirishi ma’lum [37].

D. Xu va hamkorlari in vitro tadqiqotlarida shuni ko‘rsatdiki, polistiren NP Caco-2 ichak epiteliy hujayralari tomonidan makropinositoz va klatrin vositalangan endotsitoz orqali so‘riladi va hujayralararo zich bog‘lanishning diffuziya qarshiligini buzadi, bu esa paratsellulyar moddalar transport tezligini o‘zgartiradi.

MP va NP zarrachalarining organizmga kirgandan keyingi taqsimlanishi faol o‘rganilmoqda [38]. O‘pka va ichak – tashqi muhit bilan bevosita aloqa qiluvchi eng muhim organlardir. O‘pkadan katta MP zarrachalari muko-tsiliyer tozalash orqali chiqariladi, juda mayda zarrachalar (<1 μm) esa bronx epiteliy va endoteliy hujayralar orqali qon tizimiga kiradi [39, 40]. Endotsitozdan so‘ng MP hujayra faoliyatini inhibe qiladi, hujayra siklini bloklaydi, apoptozni rag‘batlantiradi va yallig‘lanish bilan bog‘liq genlar ifodasini oshiradi [41].

MP va NP organizmga og‘iz orqali kirganda oshqozon-ichak traktida (OIT) to‘planadi [42]. 150 μm dan katta MP zarrachalari so‘rilmaydi, ichak shilliq qavati bilan bog‘lanib, epiteliy hujayralarining apikal qismi bilan kontaktga kiradi. Kichikroq zarrachalar (<150 μm) esa shilliq to‘siqni yengib o‘tishi mumkin. MP va NPning so‘rilishi o‘lchamga qarab bir nechta mexanizmlar orqali sodir bo‘ladi: endotsitoz – enterotsitlar orqali, transitsitoz – M-hujayralar orqali, persorbsiya – enterotsitlar yo‘qolgan joydagi “yoriqlar” orqali va paratsellulyar transport [38]. Zich hujayra-barrier buzilmagan holda endotsitoz, transitsitoz va paratsellulyar diffuziya orqali mikrozarrachalarning so‘rilishi sichqonlarda kuzatilgan [43, 44]. MP va NP autofagiyani ham rag‘batlantirishi mumkin [45].

Ichak immun tizimi miyeloid, limfoid va T-hujayralardan iborat bo‘lib, ularning aksariyati ichak pilakchasida va mezenterik limfa tugunida joylashgan. Peyer pilaklari yetarlicha M-hujayralarni o‘z ichiga oladi va MP hamda NPning asosiy so‘rilish joyi hisoblanadi [46]. Endotsitoz qilingan MP va NP hujayra ichidagi retseptorlar va signal uzatishni o‘zgartirishi mumkin [25, 47, 48].

Ammo enterotsitlar tomonidan mikrozarrachalarning so‘rilishi cheklangan [49]. In vitro tadqiqotlarida 60 nm o‘lchamdagi musbat zaryadlangan polistiren NP epiteliy hujayralari LS174T, HT-29 va Caco-2 bilan o‘zaro ta’sir ko‘rsatdi. NP hujayralarning yashash qobiliyati va apoptoziga sezilarli ta’sir ko‘rsatishi aniqlangan [50].

Mikro- va nanoplastiklarning immun tizimga ta’siri

Tug‘ma immunitet – patogenlarga qarshi birinchi himoya chizig‘i. Makrofaglar va neytrofil leykotsitlar antigenlarni fagotsit qilib, adaptiv immunitet hujayralariga taqdim qiladi [51]. Interleykinlar oilasi bu jarayonda muhim rol o‘ynaydi [52].

Tug‘ma immunitet hujayralarini (makrofaglar, monotsitlar, NK hujayralari) epigenetik dasturlash “tug‘ma immun xotirasi”ni hosil qiladi [53, 54]. Nanoparrachalar

TLRlarni faollashtirib, makrofaglarda pro-yallig‘lanish sitokinlari (interferon, IL-6, TNFα) ishlab chiqarilishini kuchaytiradi va regulyator sitokinlar (IL-10)ni bostiradi [33].

MP va NPning tug‘ma immunitet xotirasiga ta’siri – yangi tadqiqot sohasi bo‘lib, u plastik zarrachalarning inson organizmi bilan o‘zaro ta’sir mexanizmini aniqlash va potensial terapevtik qo‘llanmalarni ishlab chiqishga imkon beradi.

Makrofaglar organizmni patogenlar va toksik moddalardan himoya qiladi hamda to‘qima gomeostazini saqlashda muhim rol o‘ynaydi [55]. MP va NP makrofaglarni faollashtirib, oksidlovchi stress, IL-17 signali orqali apoptozani kuchaytiradi va shuning natijasida ularning toksik ta’siri ortadi [56].

Makrofaglarning ikki turi mavjud: M1 (proyallig‘lanish) va M2 (yallig‘lanishga qarshi) [57]. MP va NP M1 makrofaglarini faollashtirib, M2 faoliyatini susaytirishi aniqlangan [58]. Bu jarayon interferon γ (IFN-γ), IL-1β, TNFα, IL-6, IL-10, IL-33 va boshqa sitokinlar orqali boshqariladi [59].

MP va NP oksidlovchi stressni kuchaytiradi, reaktiv kislorod shakllari (ROS) va shikastlanish molekulalari (DAMP) hosil bo‘ladi [33, 60]. ROS mitoxondriya elektron transportini buzadi va NADPH-oksidaza fermentlarini faollashtiradi [61]. DAMP tug‘ma immunitetni faollashtirib, TLRlarni ishga tushiradi va yallig‘lanish kaskadini boshlaydi [62].

MP va NP granulotsitlar va makrofaglar tomonidan yutilganda hujayra ichidagi signal yo‘llari buziladi, bu immun gomeostazni o‘zgartirib, to‘qima va organlar shikastlanishiga olib keladi[63, 64].

Yallig‘lanish jarayoni proyallig‘lanish sitokinlari (IFN-γ, TNFα, IL-1β, IL-6, IL-33) ekspressiyasining oshishi va yallig‘lanishga qarshi sitokinlar (IL-4, IL-10, TGF-β1) ekspressiyasining kamayishi bilan bog‘liq. Bu STAT3, NF-κB va cGas/STING yo‘llarini faollashtiradi va DAMP molekulalarining ko‘payishiga, aseptik yallig‘lanish boshlanishiga sabab bo‘ladi [31, 58, 65]. Shu bilan birga T-reg limfotsitlar faoliyati susayadi va Th-2 hujayralari sitokin ishlab chiqarishi kamayadi [66].

Jigardagi ta’siri: C57BL/6J sichqonlarga 4 hafta davomida 0,5 μm o‘lchamdagi MP berilganda, jigarda NK-hujayralar va makrofaglar infiltratsiyasi oshgan, B- va T-limfotsitlarga esa ta’sir kuzatilmagan. Proyallig‘lanish sitokinlari makrofaglar va NK-hujayralar orqali oshirilgan [58].

Ichak tizimiga ta’siri: Polistiren MP 0,5–50 μm o‘lchamda 5–6 hafta davomida sichqonlarga berilganda ichak shilliq sekretsiyasi kamaygan [67, 68]. Shu bilan birga ion transporti bilan bog‘liq genlar va ileumda Ano1 geni ekspressiyasi kamaygan. Polietilen MP ta’sirida esa yo‘g‘on ichak va o‘n ikki barmoqli ichakda yallig‘lanish belgilari oshgan.

Muammoni hal qilish yo‘llari:

Mikro- va nanoplastiklarning immun tizimga ta’sirini kamaytirish uchun avvalo ularning organizmga kirish yo‘llari va biologik ta’sir mexanizmlarini chuqur o‘rganish zarur. Tadqiqotlarda MP va NP hujayra darajasida oksidlovchi stressni kuchaytirishi, proyallig‘lanish sitokinlari ishlab chiqarilishini oshirishi va immunoregulyatsiyani buzishi aniqlangan. Shu sababli ularning hujayra signal yo‘llari orqali ta’sirini aniqlash muhim hisoblanadi.

Bundan tashqari, MP va NP ning oshqozon-ichak tizimiga ta’sirini, ichak mikroflorasi va immun hujayralar faoliyatiga ta’sir mexanizmlarini eksperimental tadqiqotlar orqali baholash zarur. Maqolada qayd etilganidek, mikro- va nanoplastiklar surunkali aseptik yallig‘lanishni keltirib chiqarishi mumkin, shuning uchun yallig‘lanish jarayonlarining rivojlanish sabablarini aniqlash ham muhim ilmiy vazifa hisoblanadi.

Shuningdek, MP va NP ning organizmga uzoq muddatli ta’sirini, ayniqsa immun tizimi va reproduktiv tizim faoliyatiga ta’sirini baholash uchun qo‘shimcha eksperimental va klinik tadqiqotlar o‘tkazish zarur. Ularning zararli ta’sirini aniqlashda qonda IgA darajasi kabi biomarkerlardan foydalanish ham muhim ahamiyatga ega.

Xulosa

MP va NP ning immun tizimga ta’sirini o‘rganish bo‘yicha olib borilgan tadqiqotlar natijalari shuni ko‘rsatadiki, ular organizmda aseptik surunkali yallig‘lanish rivojlanishiga olib kelishi mumkin. Shu sababli yallig‘lanish jarayonlarining sabab va mexanizmlarini yanada chuqur o‘rganish zarur.

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